Glucose Levels Tied to Liver Transplant Outcomes

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ORLANDO — Intraoperative glucose levels were often "undesirably high" among orthotopic liver transplant recipients in a 5-year, retrospective study at Tufts Medical Center in Boston.

These glucose levels, and their fluctuations, directly affected the probability of mortality and the length of stay in the surgical ICU, the researchers found.

In addition, "these effects were pronounced in diabetics," Dr. Roman Schumann said. The analysis included 86 liver transplant recipients, 20 of whom had a history of diabetes mellitus.

Although control of glucose levels during cardiac surgery is well studied (Anesth. Analg. 2008;107:51-8; Ann. Intern. Med. 2007;146:233-43), data are limited regarding links between glycemic control and outcomes in patients undergoing orthotopic liver transplantation.

For that reason, Dr. Schumann and his colleagues looked at mean and peak glucose levels and variability of glucose levels, as well as insulin administration, in the years prior to adoption of an intraoperative glucose control protocol at Tufts.

They found a mean intraoperative glucose level of 187 mg/dL among nondiabetic recipients and 213 mg/dL among the diabetic patients; the difference was statistically significant. Mean peak glucose levels, however, did not differ significantly: 262 mg/dL among nondiabetic patients and 281 mg/dL for diabetic patients.

"Mean glucoses were fairly high for all patients, and peak glucoses were very high, I would say," Dr. Schumann noted at the annual meeting of the American Society of Anesthesiologists.

"It turned out that peak glucose and variability were important for length of stay in the ICU," Dr. Schumann said. Mean glucose levels, in contrast, were not significantly associated with a longer length

of ICU stay. None of these factors was significantly associated with length of hospital stay.

Dr. Schumann was an anesthesiologist at Tufts at the time of the study. He currently works at Beth Israel Deaconess Medical Center, also in Boston.

Mean fluctuations in intraoperative glucose did not differ significantly between groups: 138 mg/dL among nondiabetic patients vs. 142 mg/dL among diabetic patients.

Not surprisingly, a lower percentage of nondiabetic patients, 38%, received intraoperative insulin, compared with 65% of diabetic patients. Length of hospital stay, time to extubation, and probability of hospital mortality did not differ significantly between those who received insulin and those who did not.

The study included 61 men and 25 women with a mean age of 52 years. Average body mass index was 28 kg/m^2. Demographic variables were similar, except diabetic recipients were older and required more time to extubation. All patients had chronic liver failure and received livers from brain-dead donors. Combined liver-kidney transplant recipients were excluded.

Glycemic control was managed at the discretion of the anesthesia team. Glucose determinations were performed hourly at a satellite laboratory in the operating room.

Dr. Schumann and his associates used a surrogate measure for probability of hospital mortality, the Simplified Acute Physiology Score (SAPS) II. They found that increasing patient age and Model for End-Stage Liver Disease (MELD) score were each significantly associated with increased probability of mortality. "All glucose values, as they increased, adversely affected SAPS score," he said.

Three patients died, Dr. Schumann said in response to a meeting attendee's question. "Only three died over 5 years?" the attendee asked. "Yes, this was a small number of patients," Dr. Schumann replied.

The retrospective design was a limitation, Dr. Schumann said during a question-and-answer session. Another limitation was that the researchers considered only intraoperative glucose levels. "There are a lot of factors besides glucose that can affect these factors, so it's a bit bold to say glucose is involved to the extent we think it may be," he said.

The study results support use of protocol-driven glycemic control during orthotopic liver transplantation, Dr. Schumann said. Precise target values remain unknown, however. Future prospective studies may be able to determine the ideal target levels, he added. ■

References: 1. U.S. Department of Health and Human Services. *The Surgeon General's Call to Action to prevent deep vein thrombosis and pulmonary embolism: 2008.* US Department of Health and Human Services, Office of the Surgeon General, 2008. **2. Hooper WC,** Evatt BL. The role of activated protein C resistance in the pathogenesis of venous thrombosis. *Am J Med Sci.* 1998;316(2):120-128. **3. Gerotziafas GT,** Samama MM. Prophylaxis of venous thromboembolism in medical patients. *Curr Opin Pulm Med.* 2004;10(5):356-365. **4. Moll S,** Mackman N. Venous thromboembolism: a need for more public awareness and research into mechanisms. *Arterioscler Thromb Vasc Biol.* 2008;28(3):367-369. **5. Geerts WH,** Bergqvist D, Pineo GF, et al. Prevention of venous thromboembolism: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). *Chest.* 2008;133(6 suppl):381S-453S. **6. Wheeler AP.** Identifying at-risk patients for venous thromboembolism prophylaxis. In: Merli GJ, ed. *Thrombosis: Prophylaxis of Venous Thromboembolism.* Bridgewater, NJ: Elsevier; 2005:9-21. **7. American Public Health Association.** Deep-vein thrombosis: advancing awareness to protect patient lives: white paper. Paper presented at: Public Health Leadership Conference on Deep-Vein Thrombosis; February 26, 2003; Washington, DC. **8. Mismetti P,** Laporte-Simitsidis S, Tardy B, et al. Prevention of venous thromboembolism in internal medicine with unfractionated or low-molecular-weight heparins: a meta-analysis of randomised clinical trials. *Thromb Haemost.* 2000;83(1):14-19. **9. Amin A,** Stemkowski S, Lin J, Yang G. Thromboprophylaxis rates in US medical centers: success or failure? *J Thromb Haemost.* 2007;5(8):1610-1616. **10. Goldhaber SZ,** Tapson VF; DVT FREE Steering Committee. A prospective registry of 5,451 patients with ultrasound-confirmed deep vein thrombosis. *Am J Cardiol.* 2004;93(2):259-262. **11. Guyatt GH,** Cook DJ, Jaeschke R, Pauker SG, Schünemann HJ. Grades of recommendation for antithrombotic agents: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). *Chest.* 2008;133(6 suppl):123S-131S. **12. Samama MM,** Cohen AT, Darmon J-Y, et al; Prophylaxis in Medical Patients with Enoxaparin Study Group. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. *N Engl J Med.* 1999;341(11):793-800. **13. LOVENOX® (enoxaparin sodium injection) Prescribing Information.** sanofi-aventis, Bridgewater, NJ. **14. Kleber F-X,** Witt C, Vogel G, Koppenhagen K, Schomaker U, Flosbach CW; THE-PRINCE Study Group. Randomized comparison of enoxaparin with unfractionated heparin for the prevention of venous thromboembolism in medical patients with heart failure or severe respiratory disease. *Am Heart J.* 2003;145(4):614-621. **15. ENOXACAN Study Group.** Efficacy and safety of enoxaparin versus unfractionated heparin for prevention of deep vein thrombosis in elective cancer surgery: a double-blind randomized multicentre trial with venographic assessment. *Br J Surg.* 1997;84(8):1099-1103. **16. Colwell CW Jr,** Collis DK, Paulson R, et al. Comparison of enoxaparin and warfarin for the prevention of venous thromboembolic disease after total hip arthroplasty: evaluation during hospitalization and three months after discharge. *J Bone Joint Surg Am.* 1999;81-A(7):932-940. **17. Fitzgerald RH Jr,** Spiro TE, Trowbridge AA, et al; Enoxaparin Clinical Trial Group. Prevention of venous thromboembolic disease following primary total knee arthroplasty: a randomized, multicenter, open-label, parallel-group comparison of enoxaparin and warfarin. *J Bone Joint Surg Am.* 2001;83-A(6):900-906.