

# Long-Term Study Sheds Light on Neonatal NEC

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COLORADO SPRINGS — Bowel function was normal in up to 90% of patients 15-35 years after treatment for neonatal necrotizing enterocolitis in a large single-center series, but neurologic and respiratory complications were common, Dr. Thomas R. Weber said at the annual meeting of the Western Surgical Association.

The high prevalence of chronic neurologic and respiratory problems was “probably the most disturbing finding in the study,” he said, adding that blindness, deafness, and severe cerebral palsy resulted in some cases.

The incidence of neonatal necrotizing enterocolitis (NEC) has climbed in recent decades in tandem with improved survival following premature birth. Its etiology is multifactorial and poorly understood. Although today NEC is successfully managed nonoperatively in 50%-60% of cases with a combination of bowel rest, antibiotics, and ventilator support, the condition nonetheless remains a common pediatric surgical emergency, said Dr. Weber, professor of surgery and head of the division of pediatric surgery at Albany (N.Y.) Medical College and surgeon-in-chief at Children’s Hospital of Albany.

Of the 255 patients with NEC who were treated operatively and 180 who were managed nonoperatively at Children’s Hospital during 1970-1990, Dr. Weber and his coinvestigators were able to locate and survey 63% of the patients or their families.

He hypothesized that overall survival as well as long-term bowel, respiratory, and neurologic outcomes would be better among patients treated in the 1980s than the 1970s because of advances in patient management. However, outcomes were similar for patients treated in either decade.

Overall survival, for example, was 97% at follow-up among patients who were managed operatively and 88% in those who were treated nonoperatively during the 1970s, and 91% and 85%, respectively, during the 1980s—statistically similar results.

In the subset of children with NEC and a birth weight below 1,000 g, however, survival at follow-up was substantially worse (60%-75%). “There’s a significant increase in morbidity, too. Many of these infants had chronic respiratory and/or neurologic morbidity,” he said.

Roughly 90% of operatively managed patients and three-quarters of those managed nonoperatively were on a regular diet at follow-up, regardless of the decade in which they were treated. A normal bowel habit was reported by 84%-90% of patients. Nearly one-quarter of patients whose NEC was managed operatively underwent additional abdominal surgery later in life.

Neurologic deficits were present at follow-up in 25%-32% of patients, with no significant differences between groups or time periods. “We weren’t able to demonstrate any impact of operation on neurologic outcomes, and this has been the experience at a number of other centers,” Dr. Weber noted. Respiratory morbidity was present in 39%-50% of patients at 15- to 35-year follow-up.

One in five patients with NEC had short bowel syndrome. Morbidity and mortality in this subgroup were particularly high. Many of the late deaths resulted from liver failure, including several patients who had previously undergone liver transplantation or small-bowel transplantation.

Dr. Weber was surprised at how little understanding many patients and their families had about the past life-threatening condition. “A number of patients knew they had a scar on their abdomen but had no

idea what that scar was there for,” he said.

Discussant Dr. Karen W. West commented that multiple studies indicate that babies requiring care in a neonatal ICU have as much as a one-in-three chance of ending up with permanent physical, psychological, or developmental handicaps.

“It appears the morbidities in this group mainly relate to the respiratory strategies we’ve employed. It can be hoped that a series of patients from 1990 and beyond—with the initiation of our gentle ventila-

tion techniques, tolerance of lower endotracheal pressures, and lower arterial oxygen saturation levels—may actually reduce the number of patients with visual losses and chronic lung disease,” said Dr. West, a pediatric surgeon at Indiana University, Indianapolis.

The Albany study, with more than one in three patients lost to follow-up, underscores the difficulty in performing decades-long follow-up studies in pediatric patients. ■



\* Model is for illustrative purposes only.

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Other adverse events commonly associated with insulin therapy may include injection site reactions (on average, 3% to 4% of patients in clinical trials) such as lipodystrophy, redness, pain, itching, hives, swelling, and inflammation.

Whether these observed differences represent true differences in the effects of Levemir, NPH insulin, and insulin glargine is not known, since these trials were not blinded and the protocols (eg, diet and exercise instructions and monitoring) were not specifically directed at exploring hypotheses related to weight effects of the treatments compared. The clinical significance of the observed differences in weight has not been established.

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**References:** 1. Meneghini LF, Rosenberg KH, Koenen C, Meriläinen MJ, Lüddeke H-J. Insulin detemir improves glycaemic control with less hypoglycaemia and no weight gain in patients with type 2 diabetes who were insulin naive or treated with NPH or insulin glargine: clinical practice experience from a German subgroup of the PREDICTIVE study. *Diabetes Obes Metab*. 2007;9(3):418-427. 2. Hermansen K, Davies M, Derezinski T, Ravn GM, Clauson P, Home P, for the Levemir Treat-to-Target Study Group. A 26-week, randomized, parallel, treat-to-target trial comparing insulin detemir with NPH insulin as add-on therapy to oral glucose-lowering drugs in insulin-naïve people with type 2 diabetes. *Diabetes Care*. 2006;29(6):1269-1274. 3. Klein O, Lynge J, Endahl L, Damholt B, Nosek L, Heise T. Albumin-bound basal insulin analogues (insulin detemir and NN344): comparable time-action profiles but less variability than insulin glargine in type 2 diabetes. *Diabetes Obes Metab*. 2007;9(3):290-299. 4. Phillis-Tsimikas A, Charpentier G, Clauson P, Ravn GM, Roberts VL, Thorsteinsson B. Comparison of once-daily insulin detemir with NPH insulin added to a regimen of oral antidiabetic drugs in poorly controlled type 2 diabetes. *Clin Ther*. 2006;28(10):1569-1581. 5. Data on file. Novo Nordisk Inc, Princeton, NJ. 6. Heise T, Nosek L, Rønn BB, et al. Lower within-subject variability of insulin detemir in comparison to NPH insulin and insulin glargine in people with type 1 diabetes. *Diabetes*. 2004;53(6):1614-1620. 7. Data on file. NDA21-536. Novo Nordisk Inc, Princeton, NJ.



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