Current Literature

Contributing Editor—Debra S. Kovacevich, RN, MPH, CNSN
HomeMed, University of Michigan, Ann Arbor

Effect of Pulsed Dexamethasone Therapy on Tolerance of Intravenously Administered Lipids in Extremely Low Birth Weight Infants

J Sentipal-Walerius, S Dolberg, F Mimouni, et al
Department of Pediatrics, Magee-Women's Hospital, Pittsburgh, and Department of Neonatology, Lis Maternity Hospital, Tel Aviv Medical Center, Israel

ABSTRACT: We investigated the effect of dexamethasone on parenteral lipid tolerance in 7-day-old extremely low birth weight infants (n = 28) in a randomized, double-blind trial. Serum triglycerides were measured before and after 3 days of dexamethasone or placebo treatment. Infants treated with dexamethasone responded with higher triglyceride concentrations and greater sensitivity to incremental increases in the intravenous lipid dose. (J Pediatr134:229–232, 1999)

COMMENT: Intravenous lipid emulsions may be associated with increased serum triglyceride concentrations (STC). Increases in STC depend on the lipid dose, concentration, and the presence of hypertriglyceridemia-predisposing factors. Extremely-low-birth-weight infants (ELBWI <1000 g birth weight) have reduced lipid clearance because of reduced lipoprotein lipase activity and limited adipose tissue mass. Corticosteroids possibly increase STC by increasing the synthesis of triglyceride-rich lipoproteins, reducing lipoprotein lipase activity, or altering insulin secretion.

This placebo-controlled study assessed the effect of therapeutic intravenous dexamethasone therapy on the tolerance of 20% intravenous lipids in ELBWI. The two study groups did not differ significantly at baseline. STC were measured before and after therapy. The treatment group received dexamethasone (0.5 mg/kg/d) for 3 consecutive days. Lipids were continuously infused throughout therapy. Dextrose infusion rates and lipid doses were within normal dosage ranges. Study results showed significantly higher after-treatment STC in the dexamethasone-treated infants compared with the placebo group. A dose–response relationship was observed between the lipid dose and STC in the dexamethasone group but not with placebo. Study limitations were discussed.

Study findings indicate that dexamethasone may increase STC in ELBWI receiving intravenous lipid emulsions. Monitoring STC is warranted, and reducing the lipid dose may be necessary.

Imad F. Btaiche, PharmD, BCNSP

Randomized Trial of "Slow" Versus "Fast" Feed Advancements on the Incidence of Necrotizing Enterocolitis in Very Low Birth Weight Infants

SF Rayyis, N Ambalavanan, L Wright, WA Carlo
Department of Pediatrics, University of Alabama at Birmingham

ABSTRACT: *Objective:* To determine whether the rate of feed advancement affects the incidence of necrotizing enterocolitis (NEC). *Study Design:* Prospective randomized controlled trial involving 185 formula-fed infants with birth weight 501 to 1500 g and gestational age </=34 weeks. Infants were randomized into 2 groups: "slow" (n = 98), who received 15 cc/kg/d increments (a 10-day schedule to full feeds) and "fast" (n = 87), who received 35 cc/kg/d increments (a 5-day schedule to full feeds) of Similac Special Care 20 cal/oz. Feeds were increased only if well tolerated as defined by a protocol. *Results:* The incidence of NEC (Bell stage >/=II) was similar in both groups (slow 13% and fast 9%, P =.5). The incidence of perforation (Bell stage III) was also similar in both groups (slow 4% and fast 2%, P =.8). Feeds were started at a comparable postnatal age in both groups (median age: slow 5 days and fast 4 days, P =.9). Although the neonates in the fast group attained full enteral intake earlier (median days [25th and 75th percentiles]: slow 15 [12, 21] and fast 11 [8, 15], P <.001) and regained their birth weight earlier (slow 15 [11, 20] and fast 12 [8, 15], P <.05), their ages at discharge were not statistically different (slow 47 [31, 67] and fast 43 [29, 62], P =.3). *Conclusions:* A greater than twofold difference in the rate of feed advancement from 15 cc/kg/d to 35 cc/kg/d did not affect the incidence of NEC >/= stage II. Factors other than feed advancement appear to be more important in the pathogenesis or progression of NEC. (J Pediatr 134:293–297, 1999)

COMMENT: NEC continues to be the bugaboo of enteral nutrition support in neonatal nurseries. This group was involved in a prior case-control study that showed a 16% incidence of NEC during a period in which a "fast" feeding approach was often used at their clinical center.

The authors hypothesis for this prospective study was that "slow" feed advancement would decrease the incidence of NEC. However, only 56% of the infants in the fast group actually reached full feeds in the expected 5 days; in the slow group, 47% of the group actually reached full feeds in the expected 10 days. The range of time to full feeds was not described. A thorough feeding protocol that involved checking aspirates and conducting an abdominal examination was used prior to each feed. Feedings could be held or stopped, depending on the results. Obviously, feedings were held, because approximately half of both groups did not reach target feeds in the allotted time. So a more apt title for the study would be: "Intention to Use 'Fast' Versus 'Slow' Feeding Advancements." Perhaps a

difference in the incidence of NEC in this study group was due to the establishment of a feeding protocol with a very careful evaluation of the infant prior to each feed.

Jacqueline Jones Wessel, MEd, RD, CNSD, CSP

Feeding Strategies for Premature Infants: Randomized Trial of Gastrointestinal Priming and Tube-Feeding Method

RJ Schanler, RJ Shulman, C Lau, et al
US Department of Agriculture/Agricultural Research Service, Children's Nutrition Research Center, Houston, Texas

ABSTRACT: *Background:* Data on enteral feeding management of premature infants are limited and often not the subject of randomized clinical trials. Several small studies suggest benefits from the early initiation of feeding, but do not assess the combined effects of time of initiation of feeding, tube-feeding method, and type of milk used. Either singly or in combination, these treatments may affect growth, bone mineralization, biochemical measures of nutritional status, and feeding tolerance, and, ultimately, the duration of hospitalization. *Methods:* A total of 171 premature infants, stratified by gestational age (26 to 30 weeks) and diet (human milk or preterm formula) were assigned randomly among four treatment combinations in a balanced two-way design comparing the presence or absence of gastrointestinal (GI) priming for 10 days and continuous infusion versus intermittent bolus tube-feeding. *Results:* The major outcome, time required for infants to attain full oral feeding, was similar among treatments. GI priming was not associated with any measured adverse effect and was associated with better calcium and phosphorus retention, higher serum calcium and alkaline phosphatase activity, and shorter intestinal transit times. The bolus tube-feeding method was associated with significantly less feeding intolerance and greater rate of weight gain than the continuous method. In addition, the greater the quantity of human milk fed, the lower the morbidity. *Conclusions:* Early GI priming with human milk, using the bolus tube-feeding method, may provide the best advantage for the premature infant. (Pediatr 103:434–439, 1999)

COMMENT: As the authors pointed out in the introduction to this article, there are very few studies that have experimentally determined the best methods for providing enteral nutrition in premature infants. The conventional wisdom has been that continuous-drip feedings would be better tolerated. This derives from the approach in older children that are ill and may have alteration of their normal gastrointestinal motility. However, bolus feedings are actually more physiologic. This study demonstrated that the premature infant appears to tolerate bolus feedings with better tolerance than continuous-drip feeds. The philosophical question this raises is whether "healthy" premature infants are in a disease state or an altered stage (because of their extra-utero status) of normal development.

The long-term benefits of gastrointestinal priming certainly are also logical given that the gastrointestinal enterocyte receives its sustenance from the luminal contents. It is well recognized that a lack of enteral nutrition results in mucosal atrophy. That priming is beneficial in premature infants is not a new finding, but the number of infants included in this study further validates the safety of early low-level feedings. The benefits of human milk use, further confirmed by this study, are also well documented.

This study attempts at one stroke to establish the ideal method for feeding premature infants. Although this is one of the largest studies ever reported, the authors still ended up with smaller groups than was initially apparent, as infants were randomized into four groups because of the combinations of feeding options. The major outcome of time to attain full oral feedings was not significantly different between the groups, but the benefit of improved feeding tolerance and better weight gain was apparent. The actual long-term benefits of better feeding tolerance may require larger patient numbers to document statistical differences. Nonetheless, this study gives a scientific basis for an approach to nutrition in premature infants and may also indicate a necessity to change our philosophy of care in this subset of patients.

Mark R. Corkins, MD

Total Parenteral Nutrition in the Critically Ill Patient: A Meta-Analysis

DK Heyland, S MacDonald, L Keefe, et al
Department of Medicine, Queen's University, Kingston, Ontario, Canada

ABSTRACT: *Context:* Nutritional support has become a standard of care for hospitalized patients, but whether total parenteral nutrition (TPN) affects morbidity and mortality is unclear. *Objective:* To examine the relationship between TPN and complication and mortality rates in critically ill patients. *Data Sources:* Computerized search of published research on MEDLINE from 1980 to 1998, personal files, and review of relevant reference lists. *Study Selection:* We reviewed 210 titles, abstracts, and papers. Primary studies were included if they were randomized clinical trials of critically ill or surgical patients that evaluated the effect of TPN (compared with standard care) on complication and mortality rates. We excluded studies comparing TPN with enteral nutrition. *Data Extraction:* Relevant data were abstracted on the methodology and outcomes of primary studies. Data were abstracted in duplicate, independently. *Data Synthesis:* There were 26 randomized trials of 2211 patients comparing the use of TPN with standard care (usual oral diet plus intravenous dextrose) in surgical and critically ill patients. When the results of these trials were aggregated, TPN had no effect on mortality (risk ratio [RR], 1.03; 95% confidence interval [CI], 0.81–1.31). Patients who received TPN tended to have a lower complication rate, but this result was not statistically significant (RR, 0.84; 95% CI, 0.64–1.09). We examined several a priori hypotheses and found that studies including only malnourished patients were associated with lower complication rates but no difference in mortality when compared with studies of nonmalnourished patients. Studies published since 1989 and studies with a higher methods score showed no treatment effect, while studies published in 1988 or before and studies with a lower methods score demonstrated a significant treatment effect. Complication rates were lower in studies that did not use lipids; however, there was no difference in mortality rates between studies that did not use lipids and those studies that did. Studies limited to critically ill patients demonstrated a significant increase in complication and mortality rates compared with studies of surgical patients. *Conclusions:* Total parenteral nutrition does not influence the overall mortality rate of surgical or critically ill patients. It may reduce the complication rate, especially in malnourished patients, but study results are influenced by patient population, use of lipids, meth-

odological quality, and year of publication. (JAMA 280:2013–2019, 1998)

COMMENT: Meta-analysis is a process whereby studies that appear to be similar are combined to increase the power to define a true difference between the treatment and control groups. All 26 trials in this meta-analysis compared parenteral nutrition (PN) with standard therapy (ie, no nutritional support [NS]). Although the intent of Heyland and his colleagues was to assess the impact of PN in the critically ill, the vast majority of the trials involved one particular segment: surgical patients.

It was disappointing that, even when data from 2211 patients were combined, PN was not found to have any favorable effect on mortality or morbidity. This conclusion should not have been surprising, however; one needs only to review past meta-analyses to read similar perspectives. In fact, PN has been associated with higher rates of infectious morbidity in patients undergoing cancer chemotherapy.

When Heyland et al only assessed the higher quality studies, the relative risks for both mortality and morbidity exceeded 1.0; that is, the PN may even have been of net harm. Hence, even if one believes that enteral nutrition is superior to PN in critically ill patients, one cannot thereby assume that this form of NS is better than no NS at all. One lesson to be gleaned from this meta-analysis is that future trials of critically ill patients must include a true control group, namely, one not systematically provided with any NS.

Ronald L. Koretz, MD