

Parenteral Nutrition for Critically Ill Term and Preterm Neonates: A Commentary on the 2021 European Society for Paediatric Gastroenterology, Hepatology and Nutrition Position Paper

Johannes B. van Goudoever and Chris H.P. van den Akker

See “Nutritional Management of the Critically Ill Neonate: A Position Paper of the ESPGHAN Committee on Nutrition” by Moltu et al on page 274.

Most paediatric societies provide nutritional recommendations for preterm infants (1–6), although these do usually not specifically address requirements during additional intermittent critical illness apart from prematurity, such as necrotizing enterocolitis or fulminant sepsis. In this issue of *Journal of Pediatric Gastroenterology and Nutrition*, the European Society for Paediatric Gastroenterology, Hepatology and Nutrition-Committee on Nutrition (ESPGHAN-CoN) reviewed relevant studies on nutritional support in critically ill preterm and term neonates (7). The ESPGHAN-CoN advised cautiously and slightly different from previous guidelines for preterm infants despite the fact not many experimental studies have been conducted, which deviated from the existing guidelines on ‘healthy’ preterm infants as cited above.

Nutritional management in critically ill neonates and children gained much more attention after a large trial in critically ill neonates and older children (“PEPaNIC trial”) was published a few years ago (8). This multicentre RCT included 1440 critically ill children and randomized between early versus late parenteral nutrition after admission during critical illness. It turned out that withholding parenteral nutrition during the first entire week, even though enteral nutrition was less than 80% of the prescribed goal, was clinically superior to providing supplemental parenteral nutrition within 24 hours of admission (8). Secondary analyses of the PEPaNIC trial showed that withholding parenteral nutrition was also beneficial in the 209 included term neonates (9), although withholding parenteral nutrition in term neonates was also associated with increased risk of hypoglycaemia. It must be, however, stressed that no preterm infants were included in the study.

On the basis of this study, the 2018 paediatric parenteral nutrition guidelines from 4 different international nutritional societies, stated cautiously that “withholding parenteral nutrition, including amino acids, for 1 week in critically ill term infants while

providing micronutrients can be considered” (10). Now, in the accompanying article (7), the ESPGHAN-CoN decided not to make a dramatic change in those recommendations, although the interpretation is different as there is an active recommendation albeit during a shorter time span: “In critically ill term neonates, initiation of parenteral nutrition within 24 hours is not routinely recommended. However, considering the limitations of the PEPaNIC trial and the observed low risk of long-term harm from early parenteral nutrition in critically ill neonates, the ESPGHAN-CoN does not support a change towards withholding parenteral nutrition support for 7 days as standard nutritional care.” Instead, the present position paper does suggest careful initiation of parenteral nutritional support in critically ill term neonates after 48–72 hours on an individual basis and that parenteral nutrition support can be delayed until day 8 in term infants with normal nutritional state and low risk of nutritional deterioration. That statement deserves attention.

Loss of weight during the initial week of pediatric intensive care unit (PICU) admission, measured reliably only in a subset of the whole study population of 470 children with a median age of 5 months, was associated with worse clinical outcomes. Withholding supplemental parenteral nutrition during the first week, however, did not aggravate weight *z* score deterioration during PICU stay (11). In the entire group of children, withholding parenteral nutrition for 1 week did not affect survival, anthropometrics, or health status at follow-up visits 2 years after PICU admission but did improve certain domains of neurocognitive development (12). Interestingly enough, the positive effects of withholding parenteral nutrition for 1 week on long-term neurocognitive outcome, were much less seen in those (term-born) infants <1 month of age (13).

The ESPGHAN-CoN decided that is hard to base a recommendation on 1 trial only. That is a wise decision. Although the design was multicentre and included many young subjects, included patients differed quite substantially from those admitted in many neonatal units around the world. The routine nutritional management in many units might differ as well from the management as was indicated for the control group. The PEPaNIC trial did, however, open our eyes. Up till recently, as clinicians we are often trying forcefully to restore anabolism in any infant who is admitted to our neonatal intensive care unit. Being somewhat more reluctant in the acute phase of severe inflammatory illness might well be the way to go, as also suggested for preterm infants in the accompanying article (7). Nonetheless, we desperately need more of such very well executed randomized trials investigating delayed initiation of parenteral nutrition during inflammatory diseases (14,15). We should then aim to specifically include preterm neonates, who suffer from additional critical illness like sepsis or undergo surgery. At the end, such trials and not expert opinions should guide our nutritional management.

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From the Department of Pediatrics, Amsterdam UMC, University of Amsterdam, Vrije Universiteit, Emma Children’s Hospital, Amsterdam, The Netherlands.

Address correspondence and reprint requests to Johannes B. van Goudoever, Meibergdreef 9, PO box 22660, 1100 DD Amsterdam, The Netherlands (e-mail: h.vangoudoever@amsterdamumc.nl).

J.B.v.G. is member of the National Health Council and founder and director of the National Human Donor Milk Bank in the Netherlands.

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Knowledge Translation Action is Needed to Address Problems in Adherence to Pediatric *Helicobacter* Consensus Guidelines in Clinical Practice

*†Sander Veldhuyzen van Zanten

See “Low Adherence to Society Guidelines for the Management of *Helicobacter Pylori* Among Pediatric Gastroenterologists” by Bonilla et al on page 178.

Updated evidence-based consensus guidelines on *Helicobacter pylori* infection in children were published in 2016 by the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) (1). The guidelines recommend against the use of a “non-invasive test [13C-UBT (Urea Breath Test) or *H pylori* stool antigen tests] and treat” strategy for *H pylori* infection in children, in contrast to what is advised in adults (2,3). An exception to this may be the

special circumstance when a child is investigated for immune thrombocytopenic purpura (ITP) (1). In children, the aim of investigations is to determine the cause of the patient’s gastrointestinal symptoms and not just making a diagnosis of *H pylori* infection. The work-up may include esophagogastroduodenoscopy (EGD). Testing for antibiotic susceptibility is recommended to guide the choice of treatment that will be prescribed, and follow-up testing should be done to determine whether cure of *H pylori* is achieved. An internet-based questionnaire administered in 2003 to 514 North American pediatric gastroenterologists (PGI), of whom 109 (22%) responded, found a high awareness about *H pylori* but suboptimal understanding about testing, treatment, and importance of antibiotic resistance (4).

The study by Bonilla et al (5) examined the adherence to the 2016-updated evidence-based ESPGHAN and NASPGHAN consensus guidelines on *H pylori* infection in children. They studied the management of patients with *H pylori* by pediatric gastroenterologists (PGI) in a single center and identified nonadherence to the guidelines along with significant quality control issues with *H pylori* testing (5). Bonilla et al are to be congratulated for identifying quality-of-care problems in *H pylori* management at various levels in their area. More importantly, they have embarked on a quality improvement project to address the deficiencies in adherence to the *H pylori* guidelines as well as the technical difficulties in executing high-quality *H pylori* testing. Similar studies nationally and internationally are needed to determine whether the problems identified by the study of Bonilla et al exist elsewhere, and if so how these should be addressed.

This study has several limitations. The number of physicians or variations in *H pylori* management amongst them are not mentioned, and being a single-center study, there are no comparisons to determine whether the identified deficiencies are more widespread. The new *H pylori* guidelines were published late 2016, and the periods 2013 to 2016 were compared with late 2016 to 2019 to determine adherence. It is reasonable to expect that it will take some time to adopt updated guidelines, but change over time from 2016 to 2019 was not analyzed. The study found that in 42% (93/222) of children seen by a PGI, the “test and treat” strategy with noninvasive tests was used initially. Whether this is because of the invasive nature of EGD is unknown. Subsequent EGD was performed in 33 of these 93 patients. Of the 256 patients referred by primary care physicians, 77 (30%) had noninvasive *H pylori* testing performed before referral to a PGI.

The 2016 guidelines recommend that cure of *H pylori* after treatment can be assessed using 13C-UBT or stool antigen test (1). Test results to confirm that cure was achieved were available in only 80 out of 211 (38%) of patients in this study. Additionally, 20% of patients managed by PGI underwent a second EGD, though a proportion were performed to look for other reasons. No data were provided on the reasoning for a repeat EGD, making one wonder whether there were diagnostic reasons other than *H pylori*.

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From the *Division of Gastroenterology, Zeidler Ledcor Centre, Department of Medicine, University of Alberta, Edmonton, and the †Digestive Health Strategic Clinical Network, Alberta Health Services, Alberta, Canada.

Address correspondence and reprint requests to Sander Veldhuyzen van Zanten, MD, PhD, Division of Gastroenterology, Zeidler Ledcor Centre, Department of Medicine, University of Alberta, Edmonton, Alberta T6G 2X8, Canada (e-mail: vanzanten@ualberta.ca)

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