Use of high-dose early parenteral lipid in very preterm infants

To the Editor:

We read with great interest the prospective randomized trial on use of high dose early parenteral lipid in very preterm infants by the HELP trial investigators.[1] This trial addresses the clinical dilemma regarding the optimal initial dose for lipid administration in preterm infants. The authors reported a decrease in early postnatal weight loss with higher starting dose of lipids, similar to previously published data.[2] However, we would like to highlight a few issues and request a clarification.

The primary outcome of the study was the proportion of postnatal weight loss within the first 2 weeks of life. Early postnatal weight loss mainly depends on the postnatal contraction of an expanded fetal extracellular water volume.[3,4] Extracellular fluid loss is highly variable in preterm infants and weight loss may not reliably estimate the nutritional deficit. Although the authors found a difference in primary outcome (proportion of postnatal weight loss), a lack of difference in the median time to regain birth weight undermines the clinical relevance of the same.[5] Could the later outcomes, such as extrauterine growth restriction (at 36 weeks postmenstrual age), be purely attributed to the effect of higher lipid intake in the first week of life?

Also, it is unclear as to why the timing of initiation of lipid infusion was delayed for infants in the control group. The mean age of starting lipids in the control group was 17.5 hours, compared with 13.8 hours in the experimental group. Although randomization was stratified as per birth weight, the investigators did not report the number of infants born weighing less than 1000 g. It would be interesting to know the tolerance and outcomes of the higher lipid dose in this subgroup.

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Reply

To the Editor:

We appreciate the insightful comments made by Kanwal et al about our article and the opportunity to respond. Kanwal et al discuss that postnatal weight loss mainly depends on the contraction of fetal extracellular water volume. Although we agree about the important role of extracellular water contraction, several studies show that excessive postnatal weight loss occurs mostly when energy and protein intake is inadequate and providing early adequate nutrition minimizes postnatal weight loss.[1-4] Regarding the lack of difference in the time to regain birthweight, our study was not powered to detect this difference. It is worth mentioning that infants in the intervention group had 1 day less time to regain birthweight. Although this difference is not statistically significant, it matches the reduction of 2.3% (95% CI 0.4-4.1) in postnatal weight loss in the intervention group. Preterm infants lose approximately 2% of birthweight per day in the first few days of life. Every 2% loss is generally expected to result in 1 additional day to regain birthweight.

The timing of initiation of lipid infusion was purposely earlier in the intervention group. Our central pharmacy provided the neonatal intensive care unit with a ready-to-use parenteral lipid emulsions. Infants in the intervention group received lipid emulsions soon after randomization while those in the control group followed the neonatal intensive care unit protocol where lipid emulsions is ordered in the morning and administered once received.

Infants were equally distributed between the 2 birthweight strata as per stratification method. We did not report the outcomes in each stratum given the sample size. However, we would like to highlight that maximal weight loss in infants <1000 g was lower in the intervention group (10.8% vs 13.1%) as was the incidence of extrauterine growth restriction (45% vs 73%). There was no significant difference in the incidence of hypertriglyceridemia between the 2 groups.

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Considerations for future research on celiac disease in children with functional constipation

To the Editor:

Recognition of the symptomatology associated with celiac disease will allow for earlier diagnosis and ultimately better patient outcomes. We read the report by Fifi et al and appreciate the efforts they have made to attempt to improve the early diagnosis of celiac disease.[1]

However, we propose several questions regarding the methodology of the study. The authors fail to provide evidence why children under the age of 10 years had questionnaires answered by their parents, whereas those above age 11 years were able to self-report. Previously, research has validated self-reporting tools for children as young as 6 years old.[2,3] In addition, in self-reporting scales such as the Faces Pain Scale-Revised, only children under the age of 7 years had low congruent validity.[4] This evidence indicates that at least those between the ages of 7 and 10 years could have been given the ability to self-report.

The authors did well to recruit from multiple cities in the sample group. They also identify studies in different countries, such as the Netherlands and Turkey, which produced contrasting findings.[5,6] In these alternative studies, recruitment of the participants was from a single city, yet the authors do not comment on this as a potential confounder.

Based on this, we would encourage the authors, and future researchers, to use a consistent tool across their population when reviewing future data. Any further work should also aim to consider location as a confounder before drawing results from the data. In addition, future work would benefit from considering the economic implications of undertaking further work in this area. The quoted cost of diagnosing 1 child with functional constipation with celiac disease in America from a previous decade (over $67 000) will increase with the rest of healthcare costs.[7]

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Reply

To the Editor:

We want to address their disagreement with our determination to allow only children >10 years old to self-report. In their arguments, the authors ignore that our methods followed the Rome IV Committee guidelines for the use of the official questionnaire for the diagnosis of functional gastrointestinal disorders (Questionnaire on Pediatric Functional Gastrointestinal Disorders, QPGS-IV).[1] This document recommended using the self-report questionnaire in children >10 years of age (as opposed to parental report for children <10 years old). Thus, changing the self-reporting cutoffs as the authors suggested in their letter would contradict the instructions given by the Rome IV committee that issued the questionnaires. This would not only be inappropriate but would also be counterproductive as it would not allow comparing data with other studies that have also strictly followed the instructions on the use of the questionnaire.

Next, Al-Shamaa et al comment that we compared our results with other studies that were not as representative as ours. In our effort to put our data into context, we compared our results with the current literature, which