Pediatric Nutrition
CONTINUING EDUCATION FOR CLINICIANS

Nutrition Post-Hospital Discharge

Transcript

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Health Outcomes

Sarah N. Taylor, MD, MSCR: What are our goals? I talked about the goals, the outcomes related to nutrition in the hospital. Let's think about what those goals are that we want to achieve when our babies are going home. Neurodevelopment is so critical. Our babies have so many reasons, so many exposures, diseases, that can relate to worse neurodevelopment, so anything we can do to give them extra support for their brain development, of course, is a priority for us.

Growth. You can talk about is it okay for our preterm infant to be smaller than the other children in their kindergarten class, in their middle school, high school? Possibly. We worry more about growing the brain, but how wonderful is it when we can nourish our preterm infants so that they are the same size as the other children with whom they're growing as they're getting older. And then health, and specifically talking about bone mineralization when it comes to a very preterm infant. I'll also be talking a little bit about those health outcomes that relate to breastfeeding, to maternal milk exposure, and how do we have the opportunity for our infants to continue to receive maternal milk, to be breastfed and possibly get the same benefits that are described for full-term babies.

Then that leads to some other priorities I think we need when we're sending babies home—the nutrition when babies are going home. Is it our responsibility, as NICU [neonatal intensive care unit] healthcare providers, to maximize the proportion and duration of maternal milk? So, maternal milk, our focus on maternal milk, does it stop at hospital discharge when they've avoided NEC [necrotizing enterocolitis], they've avoided sepsis, they avoided retinopathy of prematurity, they avoided bronchopulmonary dysplasia. So, whew, we don't have to worry about their intake of maternal milk anymore, or are there potential benefits? [Is there] a reason we should continue to maximize maternal milk after hospital discharge?

Breastfeeding Goals

What about the family's goals? What did that family plan to do? Did this family say we want to breastfeed for 6 months? And this is talking back during the pregnancy, what was their goal? Historically, being born very preterm completely interrupts the family's goal. If they planned to breastfeed for 6 months, for a year, for 2 years, your baby is born at 28 weeks, you're not going to breastfeed. But is there a way we, as neonatal healthcare providers, can help families achieve their goal to exclusively breastfeed at some point?

Then, discharge nutrition. Keeping it simple is difficult to do. This is a form I've used when discharging infants, with all sorts of different combinations of feeds that can be done at the time of discharge or after discharge. It's overwhelming for healthcare providers, and so it's definitely overwhelming for families.

Enriched Formulas

I'm going to start where there's the most evidence, and that is with enriched formulas. Just to be clear on the terminology because there are a few different terms that can be used for these different formulas. We have standard-term formula, which would be any of the standard formulas that are made to be given to full-term, uncomplicated, healthy infants. We have preterm formula (which is over there on the far right). That's the formula we're often feeding in the NICU. It's the 24 cal/oz, or 80 to 90 kcal/100 mL. It has extra protein and calcium and phosphorus. Then there's the postdischarge formula, sometimes it's called transitional formula. This is the formula that is more than 22 kcal/oz, or 72 to 74 kcal/100 mL, and the energy, the calcium and the phosphorus are all in between the standard-term formula and the preterm formula.

In studies comparing either the postdischarge formula or the preterm formula to the standard full-term formula, there have been studies to look at neurodevelopment. Did the enriched formulas posthospital—this is posthospital discharge, not in

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the hospital but posthospital discharge—did they relate to better neurodevelopment? So, increased energy, protein, calcium, and phosphorus, did it relate to better neurodevelopment for preterm infants?

This is a Cochrane meta-analysis of the studies that have been done. The postdischarge formula was one randomized control met the level of inclusion in this meta-analysis. It's 184 babies. There was no difference in the neurodevelopment. It ranged from lower Bayley scores to higher Bayley scores, so looking at the outcomes there. Then the same with the preterm infant formula. There was no difference. It ranged from lower to higher scores. So, we don't have, when we look at the different formulas that we can feed postdischarge, none relate to better or worse neurodevelopment.

What about feeding maternal milk? We don't have a lot of large studies when it comes to feeding maternal milk posthospital discharge. We have 3 studies. The first one was O'Connor's, Debbie O'Connor who also did the DoMINO trial. She's looked at postdischarge feeding of maternal milk. This was only 39 babies. These babies were receiving at least 80% of their feeds as maternal milk at the time of discharge. They were born between 750 and 1800 g. The intervention was, you see there, the increase in protein calories. What they were doing, they were taking powdered human-milk fortifier, the multicomponent human-milk fortifier, and adding that to 50% of the baby's daily feeds. The rest of the feeds were just maternal milk, straight maternal milk without fortification. So, half of it was straight maternal milk, that could be feeding at the breast, and then the other half had the additional packets of fortifier added to add this nutrition. When they looked at neurodevelopment for exposure to this extra nutrition compared to just receiving maternal milk, they found that there was greater visual development at 4 to 6 months, but there was no difference at 18 months and the Bayley-II scale.

There are 2 other studies that have been done. One was a large study published in 2011, 320 infants [Zachariassen et al. 2011]. They did not study neurodevelopmental outcomes at 12 months. Then the third study, the De Cunha study [2016], was 53 infants that had extra .5 g/day of protein or 20 kcal for 4 to 6 months, and they saw no difference in neurodevelopment. We really don't have any research showing improved neurodevelopment with fortifying, supplementing maternal milk posthospital discharge. We just have the 1 smaller study showing that greater visual development, but it was so small. [We] would need to also look at further visual development to see what was seen at 4 to 6 months translated to improvements later in life. But still, wonderful that at least these 2 studies looking at neurodevelopment have been done.

Impact of Maternal Milk

I showed you the feeding type isn't related to neurodevelopment, be it the type of formula or the additive to maternal milk. What about human milk in general, just in continuing an intake of maternal milk posthospital discharge? These are the studies that have been done looking at maternal milk and neurodevelopment. Brenda mentioned the first one, the Vohr study, with 773 infants showing that incremental increase of maternal milk related to neurodevelopmental outcomes.

Another study looked at outcomes at 5 years and showed improved cognitive scores with breastfeeding. You just keep going down, and you can see the different age groups, really, even up to adolescence, where 1 study of 50 infants showed the milk dose significantly associated with verbal IQ as well as some full-scale IQ in boys [Isaacs et al. 2010]. We do see, these aren't randomized controlled trials because we're not going to randomize babies to receive their own mother's milk, but in these cohort studies we consistently see improved neurodevelopment with this exposure to maternal milk.

I highlight the Horwood study [2001], which was out of Betty Vohr's group, looking at the duration of breastfeeding, and breastfeeding for > 8 months in this population of very low-birth-weight infants. Those infants had higher adjusted mean verbal IQ, 6 points higher than those with no breast milk. So, I think I'm not going to say it's the strongest level of evidence of supporting neurodevelopment through feeding maternal milk posthospital discharge, but I think there's enough here that we really should consider that potential for that exposure to be important for our very preterm babies.

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Neurodevelopment Post-Hospital Discharge

What about growth trajectory posthospital discharge? Brenda talked about growth and how it relates to neurodevelopment. I have a feeling she'll be talking about that again. That in-hospital growth we really prioritize for how it relates to brain development. We have less evidence posthospital discharge of what are the growth patterns that relate to continued improvements in neurodevelopment. There is some, but I don't have time to go through all the studies, and none of them are that ah-ha, yes, that is the answer, that is how we should grow babies to optimize the brain.

I will say, though, that I'm studying this [POGO Study], and I'm really excited. We have an ongoing cohort of 500 babies that we are recruiting at birth. We're following their growth through 1 year and looking at their 2-year neurodevelopmental and body composition outcomes to relate not only their growth patterns, but the nutrition that was associated with those growth patterns, the social determinants of health, looking at those exposures and how they relate to growth and neurodevelopment as well as disease. That's one thing that of the studies that have looked at growth posthospital discharge and how it relates to neurodevelopment, the signal that keeps coming out is that those infants who have had NEC, who have BPD, who have had more illness, that they don't grow as well as those infants who have not had those diseases. That then relates—they also have worse neurodevelopment. So, really looking at what is that best growth also for infants who had different disease exposures. So, stay tuned for those results in a few years.

Growth Parameters

Getting back to all the formula studies that have been done, let's think a little about growth parameters. We talked about neurodevelopment. Growth parameters and how the different formulas, the standard-term formula, the postdischarge formula, and the preterm formula, relate to growth parameters. This is a messy slide. We are not going to go through all these details. You don't have to memorize these for the question-and-answer session. It'd be a lot of information. But I want you to get the feel for this and how this is looking at these different formulas compared to standard formula. When there's a dark blue, that means the growth, be it the weight, length or head circumference was a greater velocity with the postdischarge or the preterm infant formula. When it's orange, that means that the growth was actually better with the standard formula rather than the enriched formulas. The gray means there was no difference. So, you see there's a lot of gray. Unfortunately, even though there's been many studies looking at the best fortifier to relate to growth parameters, the evidence is really all over the place.

The Cochrane meta-analysis has tried to pull all of that together into a summary. When we look at the postdischarge formula, the 22-cal/oz formula, compared to term formula, look at weight, length, and head circumference at different time periods, both 3 to 4 months and 6 months. The summary is there was no difference, no significant difference in any of those parameters between babies fed standard-term formula or babies fed the postdischarge formula. We have no difference in growth with that. But when we look at the standard formula compared to the preterm formula, no difference in weight, length, but in head circumference, there at the bottom, at 6 months, babies who had received preterm formula compared to standard-term formula had a greater head circumference compared to those babies. There was a better head—with the idea that the head circumference relates to brain growth—that appeared to be better. Now, this feeding of the preterm infant formula, the 24-cal formula, posthospital discharge, if anyone's done that (and I happen to definitely have), some babies need that. Other babies start to grow more in width and horizontal, and you watch their fat developing, which can be good body fat for babies, but we need to be mindful of overgrowth of these infants when we're giving such dense formula posthospital discharge, which was not part of this meta-analysis.

Maternal Milk Post-Discharge

What about the growth with babies who are being fed maternal milk posthospital discharge? The O'Connor study did show that the babies who had received half of their feeds fortified, were heavier at 12 months, they were longer, and the smaller babies had a greater head circumference. And I should have mentioned before, that was up to 12 weeks postdischarge, and

these babies were discharged at an average of 38 weeks. So, this really is about 12 weeks, 10 to 12 weeks, post-term age.

The next study was of 320 babies [Zachariassen et al. 2011], and there was no difference in growth at 12 months. Now, in that study, they took a very dense fortifier and added it to an ounce or 30 mL of milk and gave that as one kind of pasty feed per day. I'm not sure how well that was absorbed rather than giving the fortifier throughout the day. The O'Connor study did show that being exposed to the human-milk fortifier related to greater growth measured at 12 months.

Bone Mineralization

What about bone mineralization? I had mentioned the importance of calcium and phosphorus in parenteral and enteral nutrition. When does that extra need for calcium and phosphorus end? How long do our babies need that supplemental calcium and phosphorus posthospital discharge? We honestly don't know that. I wish we had more information.

I showed this slide before: why calcium and phosphorus are important for our population born early because they miss that accretion they would get at the end of pregnancy. When we look at the enriched formulas, the postdischarge, and the preterm formula, and how they relate to bone mineralization, there's really no overall difference with enriched formula. Then there's this one study, this was published by Winston Koo, that showed higher bone mineral content with the standard-term formula compared to the postdischarge formula, which doesn't make sense. Why you would get less calcium and phosphorus and protein and have better bone mineral content? But that is all the evidence we have. So, that extra calcium and phosphorus in formula has not related to better bone mineralization.

Again, Debbie O'Connor looked at this in her babies who had received human-milk fortifier intervention for 12 weeks; they did have greater bone mineral content at 12 months. Potentially, that extra calcium and phosphorus for 12 weeks relates to better bone mineral content. Again, this was a small study. The other 2 studies did not look at bone mineralization outcomes.

We're really left with—you can feed just about whatever you want to posthospital discharge! We don't have a lot of great evidence. I thought by 2023, we'd have more than we do. I'll go through a little bit more about if we don't have great evidence, what should our approach be.

This is where I bring up the importance of breastfeeding for the full-term infant. These are the health outcome risks. The decreased risk related to ever breastfeeding. Most of this was just published in the AAP, the American Academy of Pediatrics, policy statement in 2022. Some of it is from previous work, but the AAP publication had a nice review of the literature. You see the decreased risk with ever breastfeeding, and then over on the right I've highlighted the importance of sustaining breastfeeding. When there's breastfeeding for 4 months, I celebrate that, especially in the United States where we have very limited family leave, and have other reasons that it can be difficult for a family to sustain breastfeeding for more than 4 months. I celebrate lactation for 4 months. I think that's fantastic to have achieved that, but there really is more benefit with continuing to at least 6 months, and that's shown here. Specifically, I highlighted a decreased risk in lower respiratory tract infection and a decreased risk in severe or persistent diarrhea with lactating for 6 months compared to less than 4.

Then you think, okay, so what's the evidence about preterm infants receiving maternal milk posthospital discharge? You mentioned the full-term infant evidence. We can assume that our preterm infants are going to receive the same benefit as full-term infants. We don't know that for sure, but we can assume that. Certainly, people have looked at the benefit of receiving maternal milk posthospital discharge. They really haven't. And again, I can't believe in 2023 I'm saying this. We really do not have, except for those neurodevelopmental studies I showed you, a lot of work on the outcomes of preterm infants' posthospital discharge with their exposure to maternal milk.

This is really it. This was looking at the days of upper respiratory infections [Blaymore Bier et al. 2002]. These were in infants born less than 2 kg. Those that were exposed to human milk had significantly less days reported of upper respiratory infections, looking from discharge to 1 month and discharge to 7 months. This is important, of course, for our preterm infants. Respiratory illnesses can be devastating for them, but we really

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need more work to identify that benefit of increasing the duration of exposure of intake of maternal milk.

To summarize this part of the talk, what kind of nutrition posthospital discharge relates to better neurodevelopment? Potentially, maternal milk and potentially growth velocity, but there's less evidence of that compared to looking at that growth velocity prior to term age. That's why I'm doing the study of 500 infants to get a better idea of how that growth posthospital discharge relates to neurodevelopment.

When we look at growth, what nutrition posthospital discharge relates to better growth? There's greater head circumference growth with preterm formula compared to standard formula. With receiving 50% of the maternal milk feeds, having that human milk fortifier supplement for 3 months posthospital discharge and greater weight and length gain, also receiving that maternal, human-milk fortification, but that was a small study. Then when we look at other outcomes, definitely the potential for decreased risk of infection, autoimmune disease, cancer and mortality with breastfeeding because that's what we see in term infants. Greater bone mineral content with the intake of some human milk fortifier for 12 weeks compared to just maternal milk. And again, that 1 small study of less days of respiratory illness with the intake of maternal milk rather than formula. So, not much which, again, is surprising at this time that we don't have more evidence.

What should we do? I have tried to send babies home on standard-term formula. I've tried to send babies home on half of their feeds with human-milk fortifier. And when I do that, about 50% of the time when they started off as very preterm, they do not grow. They are not hitting growth targets. I think, even though these studies are very helpful, I've found it to be difficult to integrate those into my clinical care. Instead, even though this is old, I really like this statement from ESPGHAN, from our European colleagues from 2006, that we need to be monitoring growth. We need to be measuring their growth. When they're not growing well, we need to supplement. We need to breastfeed when possible, but really follow the growth and aim to supplement as needed for that individual baby to grow. Especially being mindful of those babies who are small at birth, [as] they may have more limitations.

I think the key time to focus on this growth for most babies is 40 to 52 weeks because, at some point in 40 to 52 weeks, a preterm baby who isn't limited by cardiovascular disease or respiratory disease or neurological disease, so as long as they don't have severe IVH [intraventricular hemorrhage] or PVL [periventricular leukomalacia], as long as they don't have severe BPD or cardiac disease, at some point they are going to feed to grow. And that's why we have such discrepancies in these studies of different feeding types because, at some point the lightbulb comes on and a baby will take in the volume they need to grow. So really, our supplementation is to get us to that time. Of course, that might be a longer time for babies who have respiratory or cardiovascular disease. They may need that increased nutrition for their metabolic demand or babies who are limited in their neurological ability.

So, that has become my approach to figure out what feeding type works for a family regarding does mother plan to breastfeed, do we still have maternal milk, and then also works for that infant's growth pattern. But it's unfortunately not simple. It's complicated because it ends up being individualized.

To summarize the outcomes of the nutritional needs, if you do have the good fortune that you've kept maternal milk supply until hospital discharge, you have a family who wants to continue to provide maternal milk, to optimize bone mineralization in that population. Again, the potential to add the human milk fortifier until 12 weeks. Otherwise, though, there's no real evidence of what they should take. I don't have time to go into the background of this, but I encourage you to consider monitoring babies who are just on maternal milk postdischarge, ensuring that their phosphorus levels and their vitamin D levels stay within what we would consider the range related to best bone outcomes.

Growth, again, I talked about feeding to grow with the ideal velocity being that 25- to 35-g/day in the 3 months post-term age. But some babies may need to grow more because they have more catch-up growth they need to do. Neurodevelopment at this point, just concentrating on their growth trajectory and how that may relate to their neurodevelopment. Iron stores, I just mention, keep this in mind when we get to the Q&A, but iron stores, our very preterm

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babies do need extra iron if they're just on maternal milk, so 3 to 5 mg/k/day until they're taking iron-containing foods. Then vitamin D stores, at least 400 international units [IU] per day and potentially up to 1,000 IU per day. They may need other vitamins besides vitamin D. Unfortunately, we just don't have a lot of research on that.

So, just to end with thinking about can we, as neonatal care providers, support the parents' feeding goal, what they had planned to do before their pregnancy was interrupted by preterm delivery? In the US, 84% of US families initiate breastfeeding. We know a lot of them have made that decision to breastfeed during a pregnancy. There are 3 things that have to come together. If a family says, yes, we want to breastfeed, we want to breastfeed for a year, for 2 years, we have to keep mother's milk supply up. She has to continue to make at least 500 mL/day and potentially more. We have to think about the maturation of the infant's oral ability. Some babies are able to obtain milk from the breast early on, say 32 weeks in some Swedish studies, 34 weeks, 36 weeks. Some are not going to develop that ability until more like 38 to 40 weeks. We have to keep an eye on what that infant's ability is to obtain milk from the breast. Then there are specific nutritional needs, as well. All of those things have to be considered when we say, yes, we're going to help you to sustain breastfeeding to move from gavage feeds to breastfeeding so you can sustain that posthospital discharge.

We need to know the family's feeding goal, and I ask families, what is your feeding goal from the time they're admitted to the NICU. Let's go ahead and find that out how long mom planned to give her milk, so we can make that a goal throughout the NICU stay. We have to protect that milk supply. Monitor the infant's growth closely, feed to grow, have that growth trajectory, consider the infant's other needs based on the diseases and their pattern of growth and their previous nutrition, if they have some deficits. Then, I mentioned simplification. I didn't have time to go over this, but in a study that I've done previously where we were focusing on infant growth, and we had a postdischarge clinic where we were seeing babies back 2 to 4 weeks after hospital discharge, when we went through with the families their mixing of feeds, 18% of families were mixing the feeds improperly, be it a formula or an additive to maternal milk. This is a real issue, both under- and over-nutrition and potential harm. And that is the end of postdischarge nutrition.

Abbreviations

AAP	the American Academy of Pediatrics
BSID-II	Bayley Scales of Infant Development Second Edition
BPD	Bronchopulmonary dysplasia
DoMINO	Donor milk for improved neurodevelopmental outcomes
ESPGHAN	The European Society for Paediatric Gastroenterology Hepatology and Nutrition
IU	international units
IVH	intraventricular hemorrhage
MDI	Mental Development Index
NEC	necrotizing enterocolitis
NICU	neonatal intensive care unit
PDI	Psychomotor Development Index
POGO study	Patterns of Growth and Outcomes
PVL	periventricular leukomalacia

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