

# PEDIAPOD APRIL 2023 TRANSCRIPT

## **Geoff Marsh**

Hello and welcome to PEDIAPOD for April 2023. This month we look at the association between BMI trajectories and bronchopulmonary dysplasia in very preterm infants.

BPD is the most common morbidity among infants born less than 30 weeks gestational age. Managing the nutrition of preterm infants with evolving BPD is difficult because of their hypermetabolic needs associated with postnatal growth and the increased work of breathing. Commonly, nutritional interventions are focused on achieving optimal body weight gain. However, very preterm infants with evolving lung disease often experience disproportionate growth in the neonatal period, which may contribute to the odds of developing BPD.

In this episode of PEDIAPOD, I speak to Early Career Investigator Marc Beltempo from McGill University, Montreal, Canada. He and his team performed a retrospective cohort study investigating the links between change in body mass index from birth to 36 weeks gestation and evolving bronchopulmonary dysplasia.

## **Marc Beltempo**

My name is Marc Beltempo. I am a clinician-researcher at Montreal Children's Hospital affiliated to the McGill University Health Center. And my clinical work is being a neonatologist. I was trained in North America, Quebec. And then after that, I went to do a research postdoc at Toronto and then came back to Montreal McGill, where I now work as a neonatologist. And what's been great since I've been working as a clinician researcher, is I've been with colleagues who continuously stimulate our questions in clinic and in research, and one of the clinical observations we've continuously had caring for the higher risk babies or the very preterm babies, especially those born at less than 30 weeks, is that we realized that as they're growing in the neonatal intensive care unit, they look relatively disproportionate suggesting that they seem to have more body fat than actual length as they're growing in the NICU context. And that's what led us to do this research paper because we were realizing that kids that have chronic lung disease of prematurity like bronchopulmonary dysplasia, which is something that's highly associated with extreme preterm birth, mainly because preterm babies have immature lungs at birth, they're exposed to tons of environmental factors while they're in the neonatal intensive care unit, which contribute to chronic lung damage. And when we look at these kids that have bronchopulmonary dysplasia that were preterm, they seem to have these disproportionate growth aspects when we look at them, which makes it very challenging in the neonatal intensive care unit context.

## **Geoff Marsh**

How complicated is it to manage the nutrition of very preterm infants?

## **Marc Beltempo**

Managing the nutrition of preterm infants is a challenge in itself for probably two reasons: One, what is the goal of nutrition is a big challenge- is it aiming for weight gain that's similar to what the baby would have gained when the baby was *in utero*, which is a challenge to do because they're not at the same

intrauterine environment. So achieving that may not be realistic, but we also know that under feeding our babies is not good. On top of that, we're using a combination of what's called parenteral nutrition, so IV nutrition where we control protein, glucose and lipid intake. But we're also giving enteral nutrition, milk which we're supplementing with extra protein, extra fat, extra phosphates, extra minerals et cetera. So trying to find the right input or intake for the quote unquote optimal metric, or goal we're trying to aim for is an ongoing challenge, because we're not sure on both ends what is the best situation for each baby? And that's what we're trying to figure out, we're saying maybe weight gain is not the ultimate marker of growth, maybe we should be looking at other things in a clinical context.

**Geoff Marsh**

So you noticed that disproportionate growth pattern in these extremely preterm infants and a high proportion of them go on to develop BPD. What was your hypothesis about the link between those two phenotypes?

**Marc Beltempo**

We know that the body mass index, what's called the BMI, that's used largely in adults and pediatrics, because having a higher BMI or body mass index correlates with having higher fat tissue. There are a few exceptions, but as a concept that usually correlates, and having a very, very low BMI correlates with somebody that has not a lot or even not enough fat tissue, or even lean body mass. So our initial hypothesis was that babies that have either of those extreme values - either increased a lot in their body mass index or decreased too much in their body mass index - will probably have a higher risk of complications while they're in the neonatal intensive care unit. And one of those potential complications is bronchopulmonary dysplasia.

**Geoff Marsh**

So you're interested in the change in BMI and evolving bronchopulmonary dysplasia in these very preterm infants.

**Marc Beltempo**

Exactly.

**Geoff Marsh**

And it was a multicenter retrospective cohort study. Just give us a brief description of the actual setup of this.

**Marc Beltempo**

So this was a retrospective cohort study looking at three institutions. We included babies that were born less than 30 weeks gestation and that survived to at least 34 weeks corrected gestational age. And over time, what we looked at is weight measurement, length measurement, head circumference and then we also looked at caloric intake every two weeks. So we looked at all these measures every two weeks till 36 weeks corrected for each infant. And then we looked at the infants that either changed their BMI, so either increased it versus decreased it, and we compared it to infants with bronchopulmonary dysplasia, versus those without bronchopulmonary dysplasia and looked at their BMI trajectories also. When we compared infants that had an increase in their BMI, so those with the

most significant increase, they had almost two times the odds of developing bronchopulmonary dysplasia. And that's mainly attributable to the fact that those kids actually did not grow in length, but gained almost the same amount of weight as kids without bronchopulmonary dysplasia. And that's despite having a similar caloric intake. And that really highlights that probably kids with evolving lung disease can't grow in terms of length in the same way. But we're continuously feeding them and giving calories that for some reason they can't transform into linear body growth.

**Geoff Marsh**

So there's clearly this altered growth pattern in children with evolving bronchopulmonary dysplasia. Which way do you see the causality going between those altered growth patterns and the BPD?

**Marc Beltempo**

Here, it's still hypothetical. There is data from one adult study that showed that people with higher fat tissue have more lung damage and are harder to ventilate. So if that translates to babies, there may be a causal aspect where kids that are accumulating more fat, we're using higher pressures on the ventilator creating more lung damage, which can increase the risk of BPD. But there's also the other aspect where we know that especially in animal models that animals exposed to chronic hypoxia tend to have altered metabolism, and they're less able to grow in terms of linear potential and for some reason, accumulate more fat. So this may also be the situation with neonates having evolving lung disease. So it's probably a bidirectional association.

**Geoff Marsh**

How can clinicians use their observation of changing BMI<sub>z</sub> scores early in life to predict outcomes?

**Marc Beltempo**

I think the take home message is that growth is not only weight gain and we have to look at the linear growth, so the length change in babies that are preterm. Using the BMI may be a potential guide to nutrition but we do need more studies on what is the optimal BMI to aim for? And what are the nutrients that could optimize the BMI? Is it increasing, for example, the protein intake that can help mitigate or improve linear growth in certain patients that we don't have good data for yet? We do know that calories are a big determinant of growth, like if you have better caloric intake, you will grow better. But again, what is growth? Is it weight gain? And are there ways to optimize linear growth by giving more protein? That's still under investigation. But we do know that a lot of kids don't have enough protein intake so that may be a component of that.

**Geoff Marsh**

And what would you like to see happen next, and the research in this field

**Marc Beltempo**

I actually have students now looking at what are the macronutrient intake determinants of linear growth in preterm babies, and there are some people doing that in animal physiology and also other groups looking at can you stimulate linear growth appropriately and how do you do that? Those are the two big questions right now.

**Geoff Marsh**

Because I suppose it's possible that you could find a way of increasing some nutrient that's a determinant of linear growth, and then increase that in these very preterm infants with evolving BPD and that might have no effect on the BPD. I suppose it's possible that they might just be coexisting phenotypes caused by something else?

**Marc Beltempo**

Exactly. But at the same time the other question, and going back to phenotypes of BPD, is at least first do no harm. So if we find something that helps either kids without BPD, and then finding the right target with kids with BPD, that's the concept of a balance- too much of something may not be good, and not enough of something may not be good. And what our study shows is that probably too much weight gain in relation to no linear growth is not good and not enough is probably not good either. So where is that middle line where it may not change the whole trajectory of the patient but at least we're trying to optimize everything we can in kids that are at such high risk of having lung disease, and where we need to optimize ventilation strategies, infection prevention measures, nutrition we're using et cetera, and that's all part of the optimization of the care of these kids and individualized medicine.

**Geoff Marsh**

Are you in general saying that you think there's potential for the way we measure growth in these preterm infants and the way we feed them, there is potential there to do better at preventing BPD?

**Marc Beltempo**

I think so. Better measuring and having better tools to assess what is good growth in babies are required. And that's a potential area where we can maybe put a small dent into the evolution of BPD. The question now is, is BMI one of those indicators? I think we need a few more studies to go towards answering- can we use it in clinical practice? And how we use it is a big question. Actually, we presented this in many other areas so we're really psyched about how it's been received. We've presented in conferences and invited guest speakers. So this was some great work with one of my master's students in nutrition, and we've already started looking to add that into our clinical practice, and since this was a multicenter study, it's kind of reached out to all those sites, so we're quite excited about it.