

# PEDIAPOD JULY 2021 TRANSCRIPT

## **Geoff Marsh**

Hello and welcome back to PediaPod for July 2021. This month, researchers revisit the association of fluid status on the risk of bronchopulmonary dysplasia in preterm infants. Over half of infants born less than 29 weeks gestational age will either die or develop bronchopulmonary dysplasia. One possible contributor to this multifactorial disease is fluid overload in the early postnatal period, which may result in increased interstitial fluid in the lungs, impaired gas exchange and higher needs of mechanical ventilation. Previous studies have shown an association between fluid retention during the early postnatal period and increased bronchopulmonary dysplasia. However, these studies used varying clinical indicators of fluid status, and were performed nearly two decades ago, meaning their results may not apply to the contemporary NICU setting, with its widespread use of surfactants and modern incubators. In this episode, we meet this month's featured Early Career Investigator Marc Beltempo from McGill University and the Montreal Children's Hospital in Canada. He and his team studied the associations between fluid balance, serum sodium concentration and weight loss with BPD among preterm infants. He started off by telling me where his career got started.

## **Marc Beltempo**

I was born and raised in Montreal, Quebec, Canada, went to Université de Montréal which is in Montreal, Quebec, where I graduated from medical school. Through medical school and through rotations, I realized that I loved working with children, and I loved working, especially with neonates and their families. And when I went into pediatrics in Quebec City Université Laval I fell in love with the interactions we had with families in the neonatal intensive care unit, where we go from having a baby that's critically ill, that's weighing barely a pound, to three months later, this baby's weighing almost five or six pounds and going home breastfeeding with the parents. So from a medical point of view it's engaging and from a human point of view, it's so valorising and engaging also. That's what led me to become a neonatal intensivist. And from there in my practice, and through my training, I met people like Dr. Bruno Piedboeuf, who is one of my mentors in Quebec City. He helped me understand that through data, through research, you can actually change the care of your patients in real time. And then from there, I did a master's in health administration and systems analysis, which then brought me to Toronto where I did a postdoc research fellowship with Dr. Prakesh Shah, who's the head of the Canadian neonatal network. And from there, I learned to use larger databases for quality improvement and for implementing and sustaining change. And then from there, I came back to McGill in 2018 and became an early career investigator with some outside salary support grants and was able to start my research program, which aims to assess care practices that are associated with better clinical outcomes.

## **Geoff Marsh**

So that brings us on to the current paper that we're also here to talk about, which involves bronchopulmonary dysplasia. What do we know about the relationship between bronchopulmonary dysplasia and postnatal fluid status? And could you define that for us as well?

**Marc Beltempo**

What's challenging with bronchopulmonary dysplasia is that it is a very multifactorial disease. So there are a lot of things that contribute to it. The concept of fluid status, having too much fluid or not enough can contribute to the lung either swelling, to lung damage, and then subsequent risk of having BPD. And what's particular in very preterm babies, particularly those born less than 29 weeks is that there are a lot of things that affect their fluids. When we talk about fluid status, we're talking about how much you're giving, how much you're peeing, so it's that balance, and how do we evaluate that clinically. So in babies we know that if you lose a lot of water, you're obviously going to lose weight. You can calculate what you're giving the baby and what the baby's peeing and pooping - that's called the fluid balance. And then the third one you can use is a measure of the sodium which, as you dehydrate, that value is going to increase in your body. There are a lot of interventions or things around the baby that will affect that fluid status. The first thing is we know that preterm babies have very thin skin so they experience a lot more - what we call - insensitive water loss, so that contributes to their dehydration. Other factors will be how much we're giving and the other factor is going to be how is the baby able to pee or not? All these factors together contribute to that early critical phase of the fluid status in babies.

**Geoff Marsh**

It isn't the first study, is it, to look at the water balance changes in the early period. I was interested to read that this is the first study to look at this for quite a long time. Why is that?

**Marc Beltempo**

Fluid balance has been a key element in the care of preterm infants for years. Over the last 20 years, there's been a lot of changes in technology we have to better help the baby not lose as much fluids. And one of those major technological changes is the incubator which can seem very simple from the outside for somebody who's young and born in the last twenty or thirty years or practiced for a few years. But we have double plexiglass incubators, which reduces a lot of the heat loss. There are radiant warmers integrated to that with what we call servo-control temperature. So essentially, the temperature is modulated by the baby's skin temperature. And added to that you have humidifiers integrated into the isolette to maintain very high humidity which can go up to 90% humidity. So you can imagine what you call your insensible water loss through your skin and through just trying to maintain your body temperature is much lower than it was, compared to 20 years ago when such technology wasn't completely perfected. And that's what's interesting in reassessing this old question, which again, prompted our group to study this locally saying, well, we don't see the same percentage weight losses that people used to see. So how can we address it now and put that into a new context?

**Geoff Marsh**

Let's hear about your study population. This was a retrospective study, but presumably using a contemporary cohort at your hospital?

**Marc Beltempo**

That's correct. So this study was based on infants born from 2015 to 2018 in a single center, which is a level three NICU with specialized care and with standards similar to most developed countries.

**Geoff Marsh**

So let's just move straight on to the results. When you compare what you found to those earlier studies, what did the fluid balance mean for the rates of bronchopulmonary dysplasia?

**Marc Beltempo**

What we found is that when you had a higher fluid balance that accumulated over the first 10 days after birth, those with a higher cumulative fluid balance had higher odds of either dying or having bronchopulmonary dysplasia. And we also looked at whether sodium was the best indicator, or was it the weight loss. In our cohort what we found was that probably the best clinical indicator that correlated with the risk of death or bronchopulmonary dysplasia was the daily fluid balance - so looking at everything you give in and everything the baby pees out. And that's a bit different, because when we looked at the fluctuations in weight, that did not correlate well with outcomes, and it was the same when we looked at the serum sodium on a daily basis, so there were no significant associations. And the third thing we did was we actually looked to assess whether the daily sodium changes correlated with the daily fluid balance, and are those markers well correlated, and they still did not correlate very well in the study we did. So there are a lot of explanations as to why they don't correlate as well. We know that for sodium - people can give sodium to babies through IV fluids so that may be one of the factors. The second factor is that you also give sodium often when you're giving drugs to babies. So when you give, let's say, an antibiotic, you have to flush it with another IV. Typically, people use saline containing water to flush those drugs back in. So that's very hard to account for. And as for the weight change, we know that probably with a baby that weighs six or seven hundred grams, that percentage weight change, like a five gram difference, which is often the balances margin of error can probably skew the results a little bit. So that's probably why in our cohort, that's what we found.

**Geoff Marsh**

So from your perspective, as a clinician, is this good news that the most reliable indicator is this kind of crude measure fluid balance in and out, is that a good thing for people on the frontline?

**Marc Beltempo**

I think it's a great thing in the sense that it brings you back to using readily clinically available data that's non-invasive, to make a clinical decision. So had found that the serum sodium is the best marker in this context, the take home message could have been well, you need to do more daily or twice daily, or three times a day blood tests to babies that are so small, and poking them to get a blood test can be a painful procedure. So what's great about calculating what goes in and what goes out is essentially you just have to calculate what's on the pump or what you're giving the baby and make sure that the bedside team weighs the diapers of the babies at the same time.

**Geoff Marsh**

Did your study go any way to finding out where you intervene? Was there a quantitative measure of this fluid balance? At which point your alarm bells should be ringing?

**Marc Beltempo**

Maybe I take one step back and one step forward to answer that question: The step back, and where we have to be very mindful, is that we showed association and every scientist knows that association is not causation. So it's hard to say that if by actively targeting lower cumulative fluid balance, you will

cause lower BPD. What we did show though, is that infants that tended to have a lower cumulative fluid balance, and we actually generated as part of the supplementary file, a full chart with percentiles of cumulative fluid balance. And typically, when you're at the 25th to 50th percentile of the fluid balance, which we showed in our paper, you have a lower risk of death or BPD. I think the next step is asking ourselves, can we actively target and maintain a fluid balanced trajectory that's associated with lower risk of BPD. So the first step now is that we're in a quality improvement and knowledge implementation aspect of trying to target that line of the 25th percentile of fluids. And if we show that we're able to actively obtain that, the second step will be asking if by doing that, we are changing the outcomes of the babies. That will be the next step as part of a randomized trial.

**Geoff Marsh**

That was Early Career Investigator Marc Beltempo from McGill University and the Montreal Children's Hospital in Canada. And that's it for this month. Please check back in August for your next edition of PEDIAPOD. I'm Geoff Marsh. Thanks for listening.