

Practical Strategies for Management of Patients with Pediatric ARDS by R. Khemani

In this World Shared Practice Forum podcast, Dr. Robinder Khemani, co-author of the PALICC-2 guidelines, discusses the real-world application of pediatric ARDS management strategies. Through a case-based conversation, Dr. Khemani shares nuanced insights on intubation timing, ventilator settings, neuromuscular blockade, and rescue therapies, including ECMO. He also introduces the REDvent trial, a novel approach to lung and diaphragm protective ventilation. This content is ideal for clinicians, respiratory therapists, and healthcare educators seeking to deepen their understanding of evidence-informed, physiology-driven care in pediatric acute respiratory distress syndrome.

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Jeff Burns 00:18

Welcome to the World Shared Practice Forum Podcast on OPENPediatrics. I am Jeff Burns, a pediatric critical care physician at Boston Children's Hospital and Harvard Medical School. We're very pleased to have with us today. Dr. Roby Khemani. Dr. Khemani is a pediatric intensivist and the vice chair of research in the Department of Anesthesiology, Critical Care Medicine at Children's Hospital of Los Angeles and Professor of Pediatrics at the Keck School of Medicine, University of Southern California. Roby, welcome.

Roby Khemani 00:49

Thank you. Pleasure to be here.

Jeff Burns 00:51

Roby, it's been more than two years since we've had you here. I believe it was in February of 2023, when we last had you on discussing the latest updates to the PALICC-2 guidelines. And as I think everyone on the audience knows, you are one of the principal authors of the PALICC-2 guidelines, which currently guides the management of pediatric ARDS, really, not just in North America, but across the world. And we thought it would be interesting to have you on to really ask, you know, the expert behind the guidelines, how do you actually practice, you know, at Children's Hospital of Los Angeles? And I don't know if you remember, but about nine months ago, I sent out an SOS to you, when I was caring for a patient with pediatric ARDS, and said, well, wait a minute, now, what do you do here? So that's the goal of today, is to really ask an expert who writes the guidelines, how do they actually deploy these guidelines in practice? And of course, you know, let's begin with a patient with PARDS, pediatric ARDS. How do you decide when and whom to intubate with PARDS?

Roby Khemani 02:01

Yeah, that's a hard one. That's, I think one of the sort of biggest debates right now in our field is, is, how do we find this balance between who, who we can keep on some sort of non-invasive respiratory support, versus who we should intubate? And I would say that the real challenge in this area is, of course, we don't have very strong evidence. We're basing a lot of this on clinical judgment and on our expertise and extrapolation, you know, of data from from other areas. What I will say is, and I think we've all seen this in our clinical practice, there are certainly some patients that that do respond well to non-invasive respiratory support, and there are some that don't. And I think that that's part of the key

principle upon making decisions about, you know, when do you move forward and intubate a patient is what's their response to the therapy? And I think one of the biggest risks that we have is leaving a failing patient on therapy for too long, because then once they get to the point where they have to be intubated, that's less safe, right? There are more more more risk of having complications from the intubation itself. And there might be much higher risk of the patient injuring themselves during this process. This concept of patient self-inflicted lung injury, where the patient who has high amounts of respiratory effort, right, might produce stress and strain in their lung from the same ways that we might do it with how we choose to ventilate them, and that can perpetuate organ dysfunction. Now there's always this debate about whether we should use high flow? Should you use CPAP? Should you use BiPAP? And I think that we've all probably seen this in our practice, and this is what I try to employ in mind, is that this is a bit of an individual response for the patient, right? There are some patients that certainly seem to improve significantly with high flow nasal cannula. So I think to make a statement like you should not use high flow nasal cannula in patients with PARDS doesn't make sense, because there are certainly some patients that improve when they're on high flow nasal cannula. And you know, we'll think, I think about this as we move forward, and you know, you end up intubating a patient. There are certain phenotypes of ARDS, and there are patients that have more recruitable types of lung disease and less recruitable types of lung disease. And I think that high flow nasal cannula might, in fact, have a reasonable role in these patients that have high respiratory drive without a lot of recruitability to their lung. And there's a good number of those patients that we see in our practice, so they may benefit from the high flow nasal cannula, just from a dead space washout that we get with using such high flow rates, right, reduces their respiratory drive, and they clearly have a good response to it. And then there's the patients that don't where, maybe, you know, lung recruitment is their primary problem, right? They've got more collapse. And so here the positive pressure is really what we need to do for those patients where, then, you know, you think about CPAP or BiPAP. But I think the main point right is that no matter which of these therapies you're doing, you have to look at how they're responding. And if you've got a patient that does not have a very clear improvement in a short period of time of initiating these therapies, you know, within 30 minutes, within one hour, they're not getting better. That's the patient you don't sit on, and you should move forward and intubate them.

Jeff Burns 05:25

I like that proviso, a trial of therapy, time limited. You've got to be disciplined about that. You know I know in our own practice, I've seen this, you've got a patient who's in PARDS, and you put them on non-invasive ventilation, and they're working hard, but everyone says but they're captured. Their gas is stable and they're not getting any worse. But of course, at the bedside, they've got increased work of breathing, and I think patient self-inflicted lung injury is hard for all of us to keep in mind. The CO₂ may be stable on the gas and the respiratory rate is not going up, and the FiO₂ requirements not going up, but that patient is working really hard, and without esophageal manometry, we're just not seeing the terrible stretch that that alveolus is under. So I think that's a particular, a particularly seductive pathway to go down.

Roby Khemani 06:16

Yeah, yeah.

Jeff Burns 06:18

And as you said, nope, trial of therapy, see if you benefit. If you don't, we got to bail.

Roby Khemani 06:23

Yeah, I think you're right.

Jeff Burns 06:25

Well, after you have intubated them, what do you typically do next to determine initial ventilator settings? Where are you going to start?

Roby Khemani 06:32

So I think, like right after intubation, is the time where it's important to sort of assess the response of the patient, to really characterize, you know, what their respiratory mechanics are like. And I think you often have the advantage of doing this right after intubation, because they're under neuromuscular blockade at least most of the time, right? We use neuromuscular blockade when we intubate these patients. So really, the first thing that I do is try to get an assessment of whether this patient has recruitable lung disease or not. And as I alluded to, I think there are two or several phenotypes but the sort of clear one from a respiratory mechanic standpoint, that I think drives a lot of my decision making is to know whether this is a patient that has sort of what I would call a little bit more classic ARDS, where they have a loss of end expiratory lung volume, and the baby lung, where recruitment with, you know, higher amounts of PEEP, for example, might be beneficial. But that's not every patient with ARDS. And in fact, there are some that might have other main mechanisms of hypoxemia that you try aggressive recruitment strategies with, and in fact, you might do more harm. So that's the first thing that I do, is I do a sort of assessment of recruitability after I've intubated the patient. And what I typically do is a decremental increase and decrease of PEEP. In fact, this is what we recommend as part of PALICC guidelines, as far as trying to optimize PEEP. So I do a stepwise step up in PEEP. Generally I start at, let's say, a PEEP of 10 after intubating them, and I go up by steps of two. And what I'm doing when I'm going up is not really looking at the compliance. I am just trying to reopen the lungs, so I'm making sure that the patient is doing okay from an oxygenation standpoint, and importantly, that the hemodynamics of the patient are stable at that point. And I go up in steps of two to an upper limit that really depends on how the patient's response is. So 16, 18, 20, something like that. I set the delta p right the peak inspiratory pressure minus the PEEP, and I often use a pressure control mode here at this point to 15. So I'm trying to limit the total inspiratory pressure that the patient receives to really never go above 40 for that total inspiratory pressure. Once I get to the top, then I do the decremental PEEP titration, and I come back down in steps of two in that same way. And I'm looking at not just oxygenation, oxygenation is only part, part of the story, really there. It's the lung mechanics I'm trying to look at, you know, what's the, what's the tidal volume that that patient is receiving? As an example, when I have the same delta p to find that point where the tidal volume is best, ie, where the compliance might be best. And I that's how I typically set my initial PEEP. And I set the PEEP at the point of optimal compliance, or maybe two centimeters above that point of optimal compliance, is typically what I'll do. Then, of course, I adjust the FiO2 at that point based upon that PEEP. The tidal volume choice, I think is another one that's important and I think I really do try to operationalize the limits that we have with PALICC. From that standpoint the most important limit is the plateau pressure and the driving pressure limit. That we try to keep that driving pressure below 15 or so centimeters of water, and then you let the tidal volume be what the tidal volume is at that point. So you've got a patient with very impaired respiratory system compliance on a driving pressure of 15, you may have a tidal volume of four and a half mLs per kilo, right? In contrast, you have a patient that's got very good respiratory system compliance, right. Then on the tidal volume of 15, now you may have 8, 9, 10, mLs per kilo, right? And so when I think about what that upper limit of tidal volume is that I allow, it's

very dependent upon that driving pressure and plateau limit. So that, of course, if the patient has got very good compliance, I don't need that tidal volume, I don't need that driving pressure. I'll turn it down. But if a patient has very poor compliance, I don't turn up the driving pressure. I try to limit it to that amount. I compensate with the rate, and then tolerate the amount of permissive hypercapnia that's necessary for the patient at that time to stay within those limits.

Jeff Burns 11:06

Roby, that was just such a succinct description of how you titrate tidal volume and PEEP that is well appreciated, especially the PEEP titration. So tempting to go to the old adult PEEP table and dial in something there, and you just described very rationally how you're using both mechanics to titrate those variables. I wonder if we could move on to when you decide to use neuromuscular blockade versus when do you allow them to breathe spontaneously, and especially early on, with someone who's acutely ill with acute hypoxemic, hypercarbic respiratory failure, you know, where do you start?

Roby Khemani 11:48

Yeah, this is also a tough question that I think lacks a lot of clear evidence in certainly in pediatrics. I think there is sometimes a knee jerk, which is that if the patient is has severe hypoxemia, you know, they fall into that severe ARDS or that moderate ARDS bucket that I need to just throw a neuromuscular blockade on that patient and leave them under a muscular blockade for a long period of time. And I think that's where the risks that I sort of we talked about at the beginning of ventilators diaphragm dysfunction might really start to come into play even more, right? If I have to keep that patient under neuromuscular blockade and they have zero respiratory effort for the first three or four days, for example, of ventilation, can I even recover, you know, later in the course, or have they developed so much dysfunction at that time. And so, so I think conceptually, we need to go beyond just, you know, what is their oxygenation, to decide who we use neuromuscular blockade and even how much neuromuscular blockade we might use on that particular patient. So I go back to as the PALICC guidelines kind of outline is that you should think about the use of neuromuscular blockades when you cannot hit those lung protective limits for driving pressure right, for plateau pressure, for tidal volume that have been outlined. So I will allow the patient to start to spontaneously breathe, sort of regardless of where they are. Now, if they're on like 100% and a PEEP of 20, and you know, you're thinking about going on ECMO, of course not. But if it's if it's some reasonable FiO₂ that the patient is on, right, that they've weaned back down to, and you're able to achieve some reasonable pH with the driving pressure limits, right? Then I will allow that patient to start to breathe spontaneously. Once they start to breathe spontaneously, this is where it's really important to go to the ventilator, hands on the ventilator, and do a couple of things to make sure that that patient is ready for that right? The first thing I do is I measure their driving pressure. So I do a plateau pressure. And I think this is a common misconception that the plateau pressure, or the driving pressure should only be assessed in patients that are paralyzed or patients that are under, you know, full control of their ventilation. In fact, it's very important to assess the plateau and driving pressure on patients that are spontaneously breathing. Because when they're spontaneously breathing right, they're augmenting the pressure with their own negative pleural pressure. When you do an inspiratory hold on the ventilator and generate a plateau pressure, as long as you get a steady plateau, it reflects the true alveolar pressure, which is the combination of what the patient is pulling and what we're providing on the ventilator. So if you do that, and you see that, oh my gosh, this driving pressure is 20, this driving pressure is 25 right? That's the patient that I think, Okay, this is not the patient that I should allow, you know, to continue to have spontaneous breathing. And this is where I, you know, then either titrate in neuromuscular blockade or try to go up on sedation.

Now the reality is, is that sedation is complicated, and very few of our sedatives, I think, actually blunt the delta pressure or the tidal volume, most of the things that we use, because we don't use a lot of propofol, affects rate more than anything. So sometimes you can't get this with sedation alone, which is why you have to go to neuromuscular blockade. Where I think we have a lot of debate in our field, is this idea of how much neuromuscular blockade do you have to use? Do you need to fully paralyze the patient and take over? Or can you provide, if they're appropriately sedated, a sort of lighter amount of neuromuscular blockade, or partial amount of neuromuscular blockade, which limits the total pressure that the patient generates, but it may still promote them to have a little bit of respiratory effort. This is that alternative way to try to get at diaphragm protection. I will say that this is still, you know, in an experimental phase with trials, but that is my practice. So I don't, I don't mandate that a patient under neuromuscular blockade is fully, fully paralyzed, if they're triggering the ventilator, if their respiratory effort is in a reasonable range, I'll allow them to do that, because, in fact, you may get some diaphragm protection.

Jeff Burns 16:30

Well, once again, I have to really just congratulate you the way you succinctly brought physiology to this podcast and illuminated it because you and I were discussing before we went online that the loss of esophageal manometry, the manufacturer has gone out of business, and right now in Europe and North America, there's no clear pathway for a pediatric esophageal manometry device anytime soon. And what you just illuminated was, well, in a spontaneously breathing patient, measuring that plateau pressure is giving you insight into what's really happening in the pleural space, the transpulmonary pressure, which, of course, is what you care about, whether you're you know, no matter what's going on. And so that's just such a helpful reminder that, yeah, we may not have an esophageal catheter to measure the pleural pressure, but we can still have the important signal that we're looking for. What is the pressure within the alveolus by measuring that, that pressure on the inspiratory pause hold maneuver. Okay, so now, patient is getting worse, you're starting to think about rescue therapies. Clearly, as you noted, if you know it looks fulminant, then ECMO is what you're thinking about. But it usually doesn't—it often doesn't look that that direct a pathway that you're just sliding or you haven't, haven't quite captured. What are you thinking about in terms of rescue therapies and a patient you haven't quite captured the trajectory is still worrisome. What are you going to start thinking about adding in?

Roby Khemani 18:15

Yeah. So I think by obviously, by the time we're getting to this point, we've pulled the trigger on neuromuscular blockade because it's unlikely that in a patient that's sort of failing like this, that you're able to maintain significant amounts of spontaneous breathing in a safe way, right? We will likely be exceeding those lung protective limits. So certainly, neuromuscular blockade, you know, is sort of the given of what I will do when the patient starts to slide like this. Then, then I think it really comes down to again that this concept that I've alluded to throughout this podcast, which is like, what's the patient's response, recruitability or not? Right? So if you've got a patient that's got a little bit more of a recruitable phenotype, who, for example, when you were increasing the PEEP, there seemed to be a positive response, both from oxygenation and lung mechanics, as an example. So then that's the patient where I'm going to think about higher PEEP management and recruitment maneuvers, where I'm going to think about prone positioning. Prone positioning, I think, is, is particularly helpful in patients that have recruitable lung disease. Now interestingly, prone may help also in those without recruitable lung disease, we'll talk about that in a second. But certainly, I would be quick to go to that if they've got what

appears to be recruitable lung disease. And then there are some rescue ventilation therapies that are ultra-high PEEP strategies, whether you're an APRV user or whether you're a high frequency user. These are the patients, the patients that have recruitability would be the ones that I would think about deploying that. The patients that that don't have recruitable lung disease, and again, the way I assess that is sort of what I described at the beginning, I do those, you know, PEEP titrations, and I see what's going on with both oxygenation and lung mechanics. There may also be a role here for some advanced monitoring, like electrical impedance tomography, you know, in these areas, to understand the regional effects of what might be happening when you're turning up PEEP and whether it's recruitable. But if I've got that non-recruitable patient, that's the patient, I think about other therapies, like inhaled nitric oxide as an example, especially if refractory hypoxemia is the primary problem, where the patient's got some sort of RV dysfunction that might be contributing to the picture. I still think about prone there, because prone has this benefit of normalizing pleural pressure gradients when you put somebody in the prone positioning, so you get less regional differences in distention and less regional stress and strain in the prone position. So even though a patient may not have sort of classic recruitable lung, you might alter VQ matching adequately that at least you're not feeling like you're in a dangerous point of hypoxemia, you know, for too long. The other thing that I think is often under discussed is how permissive should we be with hypercapnia, right as an example, and what level of pH should we start to get uncomfortable? And I don't know that there is a very clear answer to this. What I will tell you is that I often will allow the pH to be seven, even as long as long as the patient doesn't have significant hemodynamic compromise. So if you've got single organ dysfunction, they're not on a lot of inotropes or vasopressors. A lot of patients can tolerate a pH of seven. Now, that's not adequate, not what's recommended as part of PALICC guidelines. But when you think about the balance between, who should I put on ECMO, versus should I see if I can ride this out, if it's just hypercapnia, for example, that the patient has and they have adequate oxygen delivery, you know, then, then that might be appropriate to just lower your threshold for the for what the pH might be. So in the nut of it, I think if none of that works right, then of course ECMO is, is the option if you are in an ECMO center and that, then that's where we would we would also deploy that at that point, although I will say that I'm not a very high use ECMO center, for sure, because we try these other therapies first.

Jeff Burns 22:32

We only have a short time left. But let me ask you this on the ECMO question, what always comes up, and that is, where are you going to park the PEEP or CPAP distending pressure for the patient on ECMO, let's assume you're on VV, patient who's got severe PARDS, where are you going to park the PEEP? Are you going to add in the phasic component to the rest settings, or are you going to be CPAPing it all the way?

Roby Khemani 23:05

Yeah, that's a tough one. I don't know the answer to that to be, to be blunt with you. I think that we really need to try to investigate this a little bit more to understand what the optimal support or setting should be when somebody is on VV ECMO, especially if you think about these VV ECMO runs that might be weeks, you know, at a time. I personally prefer to leave the lung open then allow it to fully, fully collapse, as long as I can stay within the lung protective limits that are sort of set forth in the PALICC guidelines, I will not use anywhere near a high, you know, the rate that I would use. But I will try to set PEEP to, you know, to keep the lung open if I can. And I will leave some amount of distending pressure with a low rate. I do not know that that is the right way to do things, or not, to be honest with you. And I think it depends a lot on your institutional practices for how to do this. And I think this is really

an area where we should, we should, we should try to figure this out. We should try to figure this out with some sort of trial testing, these testing, these strategies. It's challenging because there aren't that many patients, ultimately, that we put here. So being able to figure out if that is what impacts outcome, especially when you have so many other factors that likely contribute to the outcomes of a patient that's on VV ECMO for ARDS, right? It becomes complicated to be able to actually figure that out with the trial.

Jeff Burns 24:41

Well, Dr Roby Khemani, that's just a been a really succinct and really clear explanation of how you manage the patient with pediatric ARDS. Before we leave, I wonder if you could tell the audience about a study that you've recently published in the May 2025 issue of New England Journal Evidence, and it's a very fascinating study that you and your colleagues at Children's Hospital of Los Angeles just completed. Could you tell us a little bit about that?

Roby Khemani 25:12

Yeah, thanks, Jeff, happy to happy to talk about that. So that trial was a phase two randomized control trial of a ventilator strategy called REDvent, Real-time Effort Driven ventilator management. And you know, this concept has emerged, I would say, in the last five to 10 years of this idea, that when we think about ventilator management for patients with ARDS, adults and children, that really there are three sort of major types of risks. There's risk of ventilator induced lung injury. There's risk of very high patient effort or patient self-inflicted lung injury. And then there's the risk that we are overdoing it with our ventilator strategies to the point where the patients have minimal amounts of effort, and so they may develop ventilator-induced diaphragm dysfunction. The idea of the REDvent trial aligns with this concept of trying to simultaneously balance those three risks against one another to deliver something called lung and diaphragm protective ventilation, this concept that can we, you know, can we hit all three therapeutic targets? And sort of paramount to that is that we obey the lung protective principles that we've outlined in PALICC-2 as an example. Or adult Critical Care has their own versions of them. But simultaneously, if possible, we try to promote physiologic amounts of respiratory effort for patients. And so that's what the REDvent trial was targeting. It used a computerized decision support tool that was on a web based browser that was sitting at the bedside. And then we used esophageal manometry, actually to measure respiratory effort for each patient that was in the trial, and it was an RCT. So half of the patients got the REDvent intervention. Half of the patients got more like usual care, although we standardized ventilator liberation practices, which I think is a very important thing to do in randomized trials. So standard criteria for when patients met weaning criteria, when they would do a spontaneous breathing trial, and then the same criteria for passage of the spontaneous breathing trial, which was based on actually esophageal manometry, which was used in both groups. And what we found is that the use of this computer decision support tool, which, by the way, is run primarily by respiratory therapists. So the respiratory therapist is at the bedside every four hours, they would interact with the tool, and it would generate a recommendation of how to change PEEP, FiO2, ventilator rate, inspiratory pressure, and they accepted the recommendation if they agreed. If they disagreed, they talked to the attending physician about it and made a decision. And what we found is that patients in the REDvent group were more likely to meet the primary outcome, or which is length of weaning, a shorter length of weaning. This was defined as the time from the first spontaneous breathing trial to passage of a spontaneous breathing trial. In fact, about over half of patients in the REDvent group passed their first spontaneous breathing trial, compared to about 35% of patients in the usual care group, as an example. And this translated into a shorter time until SBT passage, a shorter overall

length of ventilation in the REDvent group compared to the usual care group. So this was promising, and in fact, it was the first trial, either in adult or pediatrics, that has really tested a lung and diaphragm protective ventilation strategy operationally in a trial focused on clinical outcomes. So we're certainly excited that it seems like it might help. And now we're going to pursue a larger phase three trial as we move forward.

Jeff Burns 28:51

Simply, simply extraordinary effort there. Can I ask you where are you on the phase three? Are you still organizing it?

Roby Khemani 28:59

We've actually submitted for funding. We'll see what happens with the National Institutes of Health right now, but it is pending review, and we have recruited 25 sites and about eight backup sites. They're all in the United States, unfortunately, right now, because of some limitations with funding at the moment for international sites, but we will find out, I think, in November, if it's got a favorable score. In all likelihood, we might have to resubmit, but that's the plan, at least for now.

Jeff Burns 29:33

Terrific, absolutely wonderful work. Roby, the dust is not settling on you. Roby Khemani, I so appreciate your coming on OPENPediatrics podcast, the author of the PALICC-2 guidelines in your research, you've done so much to improve the treatment and outcomes of children in severe pediatric ARDS throughout the world, and you remain one of the leaders in our field. And just as well, you're able to describe so well complex physiology in a very brief period of time. So I thank you on behalf of all of our colleagues around the world, and I'm going to give you the last word, and that is, you know, you're a very busy person, what was the last book of fiction or nonfiction that you read that you really enjoyed.

Roby Khemani 30:23

It's a good question, Jeff. So I don't know if you know this about me. I think maybe we've talked about this before. I'm a big baseball fan. Baseball is, you know, the sort of sport that I enjoy the most. My older son is really into baseball right now, and, you know, plays on a travel team, and so that, that's what consumes my weekend sometimes. But there has been a rash of arm injuries right throughout baseball that have happened in the last, you know, 20 years or so. And there's this fascinating book called "The Arm" that was actually written by an ESPN analyst, Jeff Passan, that sort of details the sort of history of Tommy John surgery and the various injuries that these baseball pitchers are getting, not just in the major league level, but even at the sort of youth level. And I just finished that book that I thought was really fascinating.

Jeff Burns 31:21

Well, I'm going to go out and get it. Roby, thanks so much.

Roby Khemani 31:25

Of course, it was a pleasure to be here.

Sarah Marcley 29:44

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Articles Referenced:

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