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eNeonatal Review
Podcast Issue

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VOLUME 8 – ISSUE 4: TRANSCRIPT

Featured Cases: Bubble CPAP—Analysis of the Evidence Base

Our Guest Author is Natalie Napolitano, Pediatric Clinical Manager for Respiratory Care Services at Inova Fairfax Hospital for Children in Falls Church, Virginia.

After participating in this activity, the participant will demonstrate the ability to:

- Describe the different theories about early CPAP and surfactant use in preterm infants,
- Identify infants who may not benefit from the INSURE method of CPAP and surfactant use, and
- Determine potential risk factors to identify infants who are more likely to fail NCPAP and require intubation.

This discussion, offered as a downloadable audio file and companion transcript, covers the important issues related to bubble CPAP in the format of case-study scenarios for the clinical practice. This program is a follow up to the Volume 8, Issue 3 eNeonatal Review newsletter—[Bubble CPAP—Analysis of the Evidence Base](#).

MEET THE AUTHOR



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Unlabeled/Unapproved Uses

The author has indicated that this presentation will include the off-label discussion of bubble CPAP.

Faculty Disclosure

Natalie Napolitano, MPH, RRT-NPS has no relevant financial relationships to disclose.

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- **Christoph U. Lehmann, MD** has indicated a financial relationship of honoraria from Mead Johnson and PediatrIX. Dr. Lehmann is also the Editor-In-Chief of Applied Clinical Informatics Journal. He serves on the Board of Directors for the American Medical Informatics Association.
- **Anthony Bilenki, MA, RRT, Edward E. Lawson, MD, Lawrence M. Noguee, MD and Mary Terhaar, DNSc, R** indicated they have no relevant financial relationships with any commercial supporters.

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MR. BOB BUSKER: Welcome to this *eNeonatal Review*TM Podcast.

eNeonatal Review is presented by the Johns Hopkins University School of Medicine, and the Institute for Johns Hopkins Nursing. This program is supported by an educational grant from Ikaria and Abbott Nutrition.

Today's program is a companion piece to Volume 8, Issue 3 *eNeonatal Review* newsletter: Bubble CPAP—Analysis of the Evidence Base.

Our guest is that issue's author, Natalie Napolitano.

This activity has been developed for physicians, nurses, and respiratory therapists caring for neonates. There are no fees or prerequisites for this activity.

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I'm **BOB BUSKER**, managing editor of *eNeonatal Review*. On the line we have with us the newsletter issue's author. Natalie Napolitano is the Pediatric Clinical Manager for Respiratory Care Services at Inova Fairfax Hospital for Children in Falls Church, Virginia.

She has no relevant financial relationship with commercial supporters to disclose, and her presentation today will include discussion of off-label uses of Bubble CPAP.

Ms. Napolitano, welcome to this *eNeonatal Review* Podcast.

DR. NATALIE NAPOLITANO: Thank you for having me.

MR. BUSKER: To help increase our understanding of the various CPAP strategies clinicians can employ, we've asked Ms. Napolitano to present some typical case scenarios. But before we do that, I'd like to ask for a quick clarification. Bubble CPAP — it's an unlabeled and unapproved treatment, but it's used in a lot of NICUs. My question is: why does it remain unapproved?

MS. NAPOLITANO: Going through the FDA approval process and some of the history of where bubble CPAP fits into that process, bubble CPAP was really a first way to deliver CPAP to infants. Bubble CPAP uses a conventional water column with flow, which creates pressure. The initial researchers tried to find ways to help deliver pressure, distending pressure, without having to intubate and use a more noninvasive mode of delivery.

Bubble CPAP was something that worked. The researchers saw the immediate positive effects and never went through an FDA approval process. It became standard of care without that FDA approval, rendering the need to go through the FDA approval process unnecessary.

Today we like to have FDA approvals and not use treatment regimens that are not FDA approved, but we are unable to go back and get approval for something like bubble CPAP because we would fall into the unethical position of doing research when we are not just to get FDA approval. What would have been done at the time to obtain FDA approval is to take some infants and give them no CPAP at all, and then give them bubble CPAP to see if it worked. In other words, we would have to do the studies that are required by the FDA, to find out that, yes, you will have better outcomes using the CPAP method.

We can't go through that process now because we know that leaving infants to struggle and not give them CPAP at all or putting them on mechanical ventilation at first and letting them be intubated for days and days does not give the best outcomes. We are unable, ethically, to go back and do that research. So bubble CPAP will essentially remain an unapproved standard of care as a method to deliver CPAP in general.

MR. BUSKER: Thank you. Now tell us about the patient scenarios we're going to talk about today.

MS. NAPOLITANO: Because the July issue literature review did not support one type of nasal CPAP over the other, I would like to talk about different uses of nasal CPAP in general for treating premature infants.

In the following case presentation of examples of treatment with nasal CPAP, we will use the same birth case with slightly different treatment approaches discussed in the literature, and we'll be able to look at the hypothesis and results of each route of treatment.

MR. BUSKER: That sounds like a good way to go. So if you would, then, give us the initial case.

MS. NAPOLITANO: A 790 gram male infant is born via emergent cesarean section at 26-4/7 weeks to a mother with one previous cesarean delivery. Her pregnancy was complicated by chorioamnionitis, and the neonate's Apgars were 4 and 6 with good respiratory effort. He is placed immediately on nasal CPAP, transported to the NICU, and given routine supportive care, including IV fluids and antibiotics. The infant improved and successfully avoided intubation after 7 days of life.

MR. BUSKER: Tell us the background of this treatment plan that avoids the need for mechanical ventilation.

MS. NAPOLITANO: This treatment plan is very similar to the famous Columbia method of placing the babies on nasal CPAP immediately at birth, avoiding intubation and mechanical ventilation 70% of the time in neonates weighing 750 to 999 grams. Columbia Hospital has some of the lowest rates of bronchopulmonary dysplasia in chronic lung disease in the nation. They have been very successful with this type of treatment methodology.

MR. BUSKER: The type of CPAP device used — what role does that play in the success of this treatment plan?

MS. NAPOLITANO: Columbia Hospital uses bubble CPAP; however, as we discussed in the July literature review, no studies have been able to reproduce their efforts and get the same results.

Various studies reviewed in the July issue used variable-flow CPAP with the same treatment plan

that also had favorable results and others did not have favorable results. So it still appears that there is no single type of nasal CPAP device, continuous flow versus variable flow, that is actually superior over the other.

MR. BUSKER: In this type of situation, what would be considered a failure of nasal CPAP — and let me define "failure" here as requiring intubation and surfactant replacement therapy.

MS. NAPOLITANO: Continuing to use Columbia as our gold standard for this treatment regimen, since they have widely published their results, they use the following criteria for consideration: Any infant who has an FIO₂ of greater than 60% to 80% oxygen; has persistent, severe hypercarbia, which they define as having a PACO₂ of 70 mm Hg and above; apnea; severe retractions on CPAP; intractable metabolic acidosis, which they also define as a base deficit of greater than 10 mEq/L; cardiovascular collapse; or neuromuscular disorder. So for any one of those categories, they would consider intubation of their infants and would consider CPAP a failure.

Other centers use a less strict set of criteria and somewhat personalize the response to the baby. This might be where we see the difference in the areas that need to be studied, because if we are unable to reproduce what Columbia does, it may be not the action of putting CPAP on, but the action of when we take CPAP off to escalate care that makes a difference in our outcomes.

MR. BUSKER: Now talking about surfactant — tell us about the hypothesis as to why the delivery of surfactant is not necessary for an infant this size and age.

MS. NAPOLITANO: To say whether it's necessary is still one of the questions in the arguments among the different treatment options. The theory on which this type of regimen is based is that the airway distension that occurs with nasal CPAP supports the airways and mucociliary actions and stimulates the production of natural surfactant sooner than if they were not on CPAP. Therefore, you do not need to give them surfactant replacement therapy because they're creating their own surfactant without the additional damage that occurs with conventional mechanical ventilation.

MR. BUSKER: Let's look at our second scenario — and again, this case is based on the same hypothetical infant.

MS. NAPOLITANO: A 790 gram male infant is born via emergent cesarean section at 26-4/7 weeks to a mother with one previous cesarean delivery. Her pregnancy was complicated by chorioamnionitis. The neonate's Apgars were 4 and 6 with good respiratory effort. He is immediately intubated, given surfactant, placed on nasal CPAP, and transported to the NICU, and given routine supportive care, including IV fluids and antibiotics. The infant improved and successfully avoided rescue intubation after 7 days of life.

MR. BUSKER: And the key difference in this scenario?

MS. NAPOLITANO: What's different about this case was, instead of placing the infant immediately on CPAP and not delivering any surfactant care, this infant was intubated, given surfactant prophylactically, and then extubated and placed on CPAP.

MR. BUSKER: If you would, tell us about this treatment plan and the theory behind its use.

MS. NAPOLITANO: This type of treatment method is referred to as the INSURE method of delivery, Intubating, giving prophylactic SURfactant Replacement, and then Extubating the baby. The theory is that we're administering the artificial surfactant ahead of time to help prevent any problems. We know that in this population at this stage of development, these infants do not have a full complement of all of the defenses of the lungs. They don't have the surfactant that is normally produced at birth since they have been born early. Delivering the surfactant ahead of time avoids decompensation of the respiratory status, which would expose them to a hypoxic state and put severe stress on their heart and brain. It is a more loving and enabling form of therapy than the sort of tough-love approach that Columbia uses.

MR. BUSKER: And the positive outcomes of the INSURE treatment method?

MS. NAPOLITANO: Those who use the INSURE method see a reduction in the need for prolonged intubation and mechanical ventilation. When these babies do need to be intubated, their time on

conventional mechanical ventilation is a lot shorter. There is also an indirect reduction in bronchopulmonary dysplasia or chronic lung disease rates by helping to jump-start the respiratory system to stand on its own and not need the supportive care and/or oxygen delivery, both of which we know cause extra damage to these premature airways.

We also see a reduction in rates of retinopathy of prematurity with a strict reduction of oxygen to maintain ordered oxygen saturation parameters, most often 85 percent to 93 percent.

MR. BUSKER: Take us to the other side of that now, what about the risks associated with INSURE?

MS. NAPOLITANO: The risks normally associated with this type of treatment method are the same that you would have in any routine intubation and any delivery of surfactant. These, however, are significant risks when they do occur. There is airway trauma if the person who is intubating is not experienced or it is a traumatic intubation, a difficult airway. You can get tracheal stenosis from any sort of a traumatic intubation, cardiac arrest, plugging of the airway with the delivered surfactant, then apnea because of the stress occurring on the baby, and severe hypoxic episodes.

Giving the surfactant floods their lungs with a foreign substance, and it takes a while for that to absorb into the airways and start to work. Some babies just don't handle this very well.

MR. BUSKER: This method of therapy, has it been reproduced past the initial INSURE study?

MS. NAPOLITANO: Yes, it has. Several studies have used the baseline treatment methodology of the INSURE study — intubating, giving prophylactic surfactant, and then extubating and placing the babies on CPAP. A lot of the subsequent supportive care has changed in these various studies, and the outcomes of these patients have given similar results or maintained the same results as in our initial study. We'll see an example of this in our next case presentation.

MR. BUSKER: And we'll return in a moment — with Natalie Napolitano from Inova Fairfax Hospital for Children.

DR. CHRISTOPH LEHMANN: Hello I'm Doctor Chris Lehmann. I'm the Director for Clinical Information Technology at the Children's Medical and Surgical Center at Johns Hopkins, and one of the Program Directors for eNeonatal Review.

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MR. BUSKER: Welcome back to our eNeonatal Review podcast. I'm Bob Busker, managing editor of the program. Our topic is bubble CPAP. Our guest is Natalie Napolitano, Pediatric Clinical Manager of Respiratory Care Services at Inova Fairfax Hospital for Children in Falls Church, Virginia.

We've been exploring the various CPAP options clinicians might choose — and we've been doing that by treating a single hypothetical patient with different methodologies. So now if you would, Ms. Napolitano, present our patient again, with a different treatment plan.

MS. NAPOLITANO: A 790 gram male infant is born via emergent cesarean section at 26-4/7 weeks to a mother with one previous cesarean delivery. Her pregnancy was complicated by chorioamnionitis. The neonate's Apgars were 4 and 6 with good respiratory effort. He is immediately intubated, given surfactant, placed on nasal CPAP, and transported to the NICU and given routine supportive care, including IV fluids and antibiotics. Within 72 hours of birth, the infant

began having apneic episodes and required re-intubation and mechanical ventilation.

The differences in treatment options in this case is, the infant was initially treated with the INSURE method — intubation, surfactant, extubation, and nasal CPAP. He failed this approach by requiring intubation within 72 hours of birth and needing to be placed on a ventilator.

MR. BUSKER: Are there ways to predict which infants will fail this initial INSURE treatment method?

MS. NAPOLITANO: A study by Cherif and colleagues in the American Journal of Perinatology in 2008¹ specifically looked at who fails this initial INSURE method and who doesn't. They used a retrospective analysis of infants ages 27 to 34 weeks' gestation who were treated with the INSURE method. Those infants were then split into two groups for analysis: those who failed the method and those who succeeded. The failure rate was 32 percent.

The goal of this study was to compare the two groups to see if there were any clear differences that would predict which method to use: Should we just use the INSURE method with these infants, or intubate them, give them a little more support for a couple of days, and extubate them because we know they are going to fail the treatment methodology and therefore cause more harm to their lungs?

Unfortunately, they were unable to find any sort of demographic predictors or characteristics of events that occurred during the birth that would let them know before starting the treatment whether infants would pass or fail the INSURE methodology.

MR. BUSKER: Let's stay with that study for a moment — and I want to remind our listeners that links to this and other studies Ms. Napolitano has mentioned can be found in the downloadable transcript version of this podcast. But in that 2008 study by Cherif and colleagues — did the authors note any similarities within the group of patients that failed the INSURE method?

MS. NAPOLITANO: Some characteristics of the condition as the infant progressed gave some indication that they were going to fail or had impending failure of the INSURE method. Those that had statistical significance were:

- average birth weight under 1,000 g
- small size for gestational age
- arterial PCO₂ of 55.4 ± 3.4 cm of water pressure
- base deficit of negative 5.3 ± 0.9 mEq/L
- AA gradient of 0.16 ± 0.05
- mean serum hemoglobin <14 g/dL

When babies fall into one, two, or even three of these categories, they may be starting to fail, and you may want to veer your treatment plan toward intubation and support instead of keeping them on nasal CPAP and waiting to see where they are going to fall out in their treatment.

One similarity we also saw that did not meet statistical significance, but was a trend to be aware of, is that rates of patent ductus arteriosus and mortality within 28 days were greater in infants who failed the INSURE study, meaning they had a PDA that needed treatment, and they died within 28 days. That means if you have a PDA that's staying open; you may want to jump toward giving a little more support or hold off and see if they can improve on their own.

MR. BUSKER: Non-pulmonary considerations that favor CPAP use instead of routine intubation for these small babies — tell us about those, if you would.

MS. NAPOLITANO: A study by Geary and colleagues² in the *Journal of Perinatology*, also published in 2008, explored the growth rates of infants who were born at less than 1,000 grams and the changes in management from intubation and conventional ventilation to initial CPAP, and how this affects babies' growth rate.

We know that when looking at bronchopulmonary dysplasia or chronic lung disease, multiple factors affect outcome rates. One factor is nutrition, which we have always looked at. In this study they discovered a reduction in days to lowest birth weight by approximately 2 days, dropping from 7 days to 5 days. This is significant, because we know babies lose weight initially as they're struggling and then start to gain back their weight. So the babies in this study began to regain weight within 5 days instead of 7 days when starting with nasal CPAP.

They also reduced the number of days required for infants to regain their birth weight. They were able to get back to baseline within approximately 4 days.

The intubation group regained in 16 days, whereas the nasal CPAP group recovered to baseline in only 12 days.

They reduced the time to initiation of enteral feeding by approximately two days — 6.5 days in the intubation group and 4.8 days in the nasal CPAP group. So they saw a significant improvement in earlier initiation of nourishment and faster weight gain in these babies, which helps them to be stronger and grow better.

MR. BUSKER: Other than CPAP versus CMV, were there other factors in the care plan that were changed?

MS. NAPOLITANO: By changing respiratory strategy from prophylactic surfactant and conventional ventilation to the INSURE method, they also lowered the goals for the oxygen saturation from >95% to 90% to 95%, and decreased their initial FIO₂ use from 60% to 40%. They used amino acid supplements on the first day of life, rather than the previous practice of dextrose- and electrolyte- containing solutions, followed by a 4 to 6 day advance of amino acids.

Nutrition has always been one of many factors we were looking at to reduce bronchopulmonary dysplasia. They did not look at ROP rates in this study and with their decrease in use of oxygen and acceptable oxygen saturation ranges, they may also have seen a reduction in those; we just didn't get a chance to see that output measure.

MR. BUSKER: Again, a reminder that links to the studies by Cherif and Geary that we've been discussing can be found in the podcast transcript on our website.

Change of subject now, Ms. Napolitano. I understand that since you wrote our July newsletter, an important new study was published in the *New England Journal of Medicine*³. Can you tell us something about that?

MS. NAPOLITANO: Yes, the study is being referred to as the SUPPORT Study Group and was performed through the Eunice Kennedy-Shriver NICHD Neonatal Network. It is a multi-centered randomized trial that was a 2-by-2 factorial design involving infants with gestational ages of 24 weeks to 27 weeks and 6 days.

The infants were randomly assigned to an intubation group that was given surfactant treatment within one hour of life, or a CPAP treatment group in which CPAP was initiated immediately at delivery, with the subsequent use of protocol-driven limited-ventilation strategies.

The infants were also randomly assigned to 1 of 2 target ranges for oxygen saturation. These two ranges were 85% to 89% or 91% to 95% until they were age 36 weeks or were no longer receiving any kind of ventilatory support.

The rates of primary outcome did not differ significantly between the CPAP group and the surfactant group, approximately 48% to 51%, respectively, for the risk of CPAP, after adjustment for gestational age, center, and familial clustering of multiples.

The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks of age, with a rate of 48.7% percent and 54.1%, respectively.

Infants who received CPAP treatment required intubation, postnatal corticosteroids, or BPD less frequently than infants who received surfactant treatment. This was a statistically significant result. They also required fewer days of mechanical ventilation and were more likely to be alive and free of need for mechanical ventilation by 7 days of life. Both of those results also had statistical significance.

MR. BUSKER: In your opinion, what does this study add to our CPAP knowledge base?

MS. NAPOLITANO: This study is significant because it compares the Columbia method of CPAP delivery immediately at birth with no prophylactic surfactant to the INSURE method, which intubates and gives surfactant, to evaluate which method is potentially better.

The study found some significant differences and no insignificant differences. It gives us a somewhat clearer picture of which method is better. There is a complication in looking at outcome ranges, which they addressed by using a 2-by-2 factorial design and two different oxygen saturation goal markers. That can also affect the outcome of BPD.

In my opinion, I would like to have seen this study done with one strict goal — the oxygen saturation outcomes — just the comparison of the two groups, without another factor in there.

MR. BUSKER: The link to that study can also be found in the transcript version of this podcast. One final question, Ms. Napolitano. Look into the future for us, if you would — what would you like to see happen?

MS. NAPOLITANO: I see the need for additional research. This tends to be our answer for everything in medical research. We have so many publications and reviews of the big things we do to care for these infants after birth and somehow try to fit them together into a better picture of what our appropriate treatment should be.

We need to focus more on some of the smaller pieces, not just how to do things, but also how to undo them. We mentioned in our first case, maybe it's not when we put the CPAP on, but when we take it off and when we choose to escalate care that may make the big difference in outcome rates for chronic lung disease in these babies.

We also looked at nutrition. This is something that we definitely need to take a closer look at. What is determined before the changes in ventilator strategies isn't something we can really carry over into our new changes of using CPAP primarily. We need to rethink how and when we start nutrition with these new immediate ventilation strategies, because these babies are burning up more calories and they need that extra oomph to grow and have energy, and they are working harder just being on nasal CPAP instead of the full support of mechanical ventilation.

In medicine there is always a reaction to every action. Every time we change something, we have to go back and redo the research. So it would be great to see the whole picture of what centers with great BPD rates and chronic lung disease rates are doing, looking at the little things they're doing, not just the big things, because that's potentially why we're unable to reproduce results in studies farther down the line.

MR. BUSKER: Natalie Napolitano, from the Inova Hospital for Children in Falls Church, Virginia — thank you for participating in this eNeonatal Review Podcast.

MS. NAPOLITANO: You are very welcome, thank you very much for the opportunity.

MR. BUSKER: This podcast is presented in conjunction with the eNeonatal Review Newsletter, a peer-reviewed, CME/CE-accredited literature review e-mailed monthly to clinicians caring for neonates.

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REFERENCES

1. Cherif A, Hachani C, Khrouf. Risk factors of the failure of surfactant treatment by transient intubation during nasal continuous positive airway pressure in preterm infants. Am J Perinatol. 2008;25(10):647-652.
2. Geary CA, Fonseca RA, Caskey MA, Malloy MH. Improved growth and decreased morbidities in < 1000 g neonates after early management changes. J Perinatol. 2008;28(5):347-353.
3. Support Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network, Finer NN, Carlo WA, et al. Early CPAP versus Surfactant in extremely preterm infants. N Engl J Med. 2010;362(21):1970-1979.