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## Epoprostenol: A Look at a Last-Line Inhalation Therapy for ARDS

### Dr. Turck:

Welcome to *Clinician's Roundtable* on ReachMD. I'm Dr. Charles Turck, and joining me today to discuss the use of inhaled epoprostenol to treat acute respiratory distress syndrome, or ARDS for short, is Dr. Justin Reinert. He's an Assistant Professor of Clinical Pharmacy at the University of Toledo.

Dr. Reinert, thanks for joining me today.

### Dr. Reinert:

Thank you so much for having me. I appreciate it. Great to be here.

### Dr. Turck:

So why don't we start, Dr. Reinert, with some background. What is acute respiratory distress syndrome, and what causes it in adults?

### Dr. Reinert:

It's a really great question, and unfortunately, it's something that is quite a complex pathology, and there are various different avenues that go into making the diagnosis of this. Of course, I am not a diagnostician by training. However, I think it's important for us as we start thinking about pharmacotherapy options to at least have a firm handle on it. So in broad terms or painting with kind of a broad stroke here, ARDS is really a clinical syndrome that results in lung inflammation and the presence of edema that leads to respiratory failure.

There's a ton of different etiologies behind this as I mentioned a few moments ago. Really though, when we consider incidence and prevalence data for ARDS, sepsis, both from pulmonary or non-pulmonary sources, seems to be the most implicated pathology behind the predisposition or the cause of ARDS, and there's an even higher tick in the column if that sepsis is originating from a pulmonary source, such as pneumonia—be that community-acquired, hospital-acquired, or ventilator-associated.

There are certainly other areas or other things as well that have been implicated in the formation of ARDS: noninfectious causes, including a traumatic injury, and some type of aspiration pneumonitis where it's really just more of an inflammatory phase. There's even been associations with transfusion-related injuries and the sometimes flash edema or pulmonary edema that is associated with that.

### Dr. Turck:

And what can you tell us about present treatment options for ARDS?

### Dr. Reinert:

So ARDS is kind of the end stage, if you will, of really poor aeration and oxygenation. Treatments for this are multifactorial. And what I will say is that this is more of a management strategy as opposed to a treatment strategy, and what I mean by that is that whatever the precipitating factor is, it's important that that underlying etiology be addressed and resolved for any meaningful hope to completely resolve ARDS, even though improvements can be made with the introduction of certain positioning, so prone positioning, be that with the bedside nurses flipping patients or using technology that can do that for patients, and then also the introduction of pharmacotherapy options. So we're certainly talking about the same medications that prescribers may be familiar with from outpatient management of asthma and COPD, but certainly, these may include long-acting anticholinergic agents or a short-acting anticholinergic medication delivered via nebulization, inhaled beta agonists, inhaled corticosteroids either alone or in combination with systemic corticosteroids, and anything that can help improve aeration with bronchodilatory-type mechanisms. And then, of course, within that family of bronchodilatory medications, we arrive at agents, such as epoprostenol.

### Dr. Turck:

So you had mentioned inhaled epoprostenol. I was wondering if you could tell us a little bit more about that.

**Dr. Reinert:**

First, maybe a little bit of background information on epoprostenol, the drug itself. Epoprostenol is actually a prostacyclin. It's sometimes known as prostaglandin or prostacyclin and prostaglandin PGI<sub>2</sub>. It is a very strong vasodilator of all the vascular beds, including the alveolar capillary barrier within the lungs, which is, of course, the source and the site where oxygen exchange happens within us as humans. It also has some inhibitory effects on platelet aggregation, which is useful potentially in this pathology, potentially some in COVID-19-associated ARDS, and there are some other off-label uses for this drug as well as ensuring patency for patients on hemodialysis or continuous renal replacement therapy.

Even though that's not our purpose here today, I think it's interesting that it has been employed for that antiplatelet activity. But nevertheless, epoprostenol is really employed somewhat as a last-line therapeutic option in patients who have experienced treatment failures or lack of improvement associated with any of those previously discussed respiratory medications—again, the long-acting anticholinergics, the short-acting anticholinergics, beta agonists, corticosteroids, what have you.

**Dr. Turck:**

For those just tuning in, you're listening to *Clinician's Roundtable* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Justin Reinert about the use of inhaled epoprostenol in acute respiratory distress syndrome, or ARDS, in adults.

So, Dr. Reinert, what else can you tell us about the safety and efficacy of inhaled epoprostenol in adult patients with ARDS?

**Dr. Reinert:**

So I'll go ahead and get started talking a little bit about the efficacy first, and then we can dive into some of the safety considerations thereafter. Obviously, we want to ensure anytime we are utilizing pharmacotherapy that it is both efficacious and safe. Unfortunately, this drug has some demerit marks on both fronts that are worth discussing. Historically, even though these medications are used as somewhat as a last-line option, they have not been associated with improvement in clinical patient outcomes. In point of fact, there really has been no clearcut evidence supporting their effect on mortality on ventilator-free days attenuation and disease severity and things of that nature.

But what epoprostenol has demonstrated is an increase in oxygenation. And this may seem a little bit counterintuitive to the point where, okay, we're breathing better, we have more available oxygen for that alveolar capillary bed exchange; however, this really goes back to the tenet that I spoke about a few moments ago where this is a disease of management where the underlying cause really needs to be resolved prior to making headway against ARDS and the ultimate resolution of ARDS.

So with that said, I'll kind of move on to some of the safety considerations that I can speak about. The other thing that I want to make sure that I mention is that the route of administration of this drug that we are delivering, these are both inhaled epoprostenol. As I mentioned earlier, there are other indications where it may be used intravenously, so some of the adverse drug effects that are listed in the package insert are much more relevant in patients whom are receiving this drug systemically as opposed to inhaled. However, they are still relevant and should raise flags and be a concern to prescribers.

Perhaps the most principal adverse drug effects associated with epoprostenol when given via nebulization include cardiovascular effects, specifically flushing. There have been incidences of tachycardia as well as hypotension and chest pain. Beyond that, there are some CNS, or central nervous system, deleterious effects that are worthwhile to consider, including significant incidents of headache, dizziness, the presence of chills, and in some cases, agitation and even paresthesias. This drug has been found to be much safer than its comparator, so given the safety data, the cost-effectiveness, and the somewhat marginal efficacy, this has really become the drug of choice when choosing to employ a last-line strategy in the management of ARDS.

**Dr. Turck:**

How do you integrate inhaled epoprostenol into the overall ARDS treatment plan? Do you typically use it in combination with other agents? What makes you decide to use it?

**Dr. Reinert:**

This is really, as I mentioned previously, a last-line agent, so these patients have already failed other interventions, including those medications we spoke about before: the long-acting or short-acting anticholinergic drugs or beta agonists, and corticosteroids, be they systemic or nebulized. These patients will be receiving optimized pharmaceutical and medical care as it relates to the management of whatever that underlying etiology may be, and only at that point, if we cannot make any headway in terms of their ventilatory status or their oxygen saturation would we consider employing a drug such as this. There are certainly some caveats to its use. Being that this is an inhaled product that also comes in an intravenous form, there are certainly issues with drug errors that have happened at the patient bedside, so we want to be cognizant of that. So it's not a decision taken lightly per se, but more rather certainly the end game, if you will,

in terms of trying to get these patients improving their oxygenation to buy a little bit of time to manage that underlying cause of that ARDS.

**Dr. Turck:**

And before we close, Dr. Reinert, are there any additional thoughts you'd like to leave with our audience today?

**Dr. Reinert:**

There are some, as I mentioned, intricacies about providing the drug just for anybody that's using this drug or choosing to deploy it at the bedside. There is special tubing, special syringes, and all sorts of special products that are necessary to compound and formulate this drug so that it is appropriate for use in the nebulization circuitry, so I encourage you to make sure that your facility has those steps in place in order to do that. There are also a couple different dosing strategies that are out there. There's both a fixed dose and a weight-based dose, each of which have data for continuous infusions.

There have been reports of some drug errors due to the provision of doses or some discrepancies in the provision of doses whereas sometimes health system electronic medical records will use a nanogram dose, which is how this drug comes, whereas others use a milliliter dose, which is how we typically measure things that go into the nebulization circuitry. So again, just taking a moment to do your due diligence and ensure that cautions are in place to ensure just the safety in providing this drug to patients I think is a well-warranted step.

**Dr. Turck:**

Well, this has been a really important discussion about an area where there are only a handful of effective pharmacotherapeutic treatment options. And I want to thank my guest, Dr. Justin Reinert, for sharing his valuable insights on the use of inhaled epoprostenol in acute respiratory distress syndrome in adults.

Dr. Reinert, it was a pleasure speaking with you today.

**Dr. Reinert:**

Thank you so much for having me. I appreciate it.

**Dr. Turck:**

For ReachMD, I'm Dr. Charles Turck. To access this and other episodes in this series, visit *Clinician's Roundtable* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.