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Cutting-Edge ALS Treatment: Helping Patients Breathe Easier

For ALS patients, the simple act of breathing is one of the greatest daily challenges. What cutting-edge treatments can help ALS patients breathe easier? Welcome to the Clinicians Roundtable on ReachMD XM157, The Channel For Medical Professionals. I am your host

Dr. Bruce Bloom and joining us to discuss Breathing Assistance for ALS Patients is Dr. Raymond Onders, Associate Professor Of Surgery at Case Western Reserve University School of Medicine in Cleveland, Ohio. Director of the minimally invasive surgery at the University Hospital at Case Western Medical Center.

DR. BLOOM:

Dr. Onders, Welcome to ReachMD.

DR. ONDERS:

Thanks for having me on your show.

DR. BLOOM:

So, start up by giving us sort of a refresher on the anatomy and physiology of breathing.

DR. ONDERS:

Oh, thank you, and this has been an active part of our research now for over a decade. What we know about breathing is that you have to have an intact muscle, the diaphragm, you have to have a nerve, the phrenic nerve going through that diaphragm, you have to have the motor neuron, the phrenic motor neuron from C3, C4, and C5, that will help fire the nerve in the muscle for contraction against the diaphragm contracture breathing. We also know that the phrenic motor neurons have some upper motor neuron signals coming from our cerebral cortex where we can take a deep breath with our diaphragm. We also have a different nighttime breathing system with our pre-box complex in the special somatic nuclei in our brain stem that controls our nighttime breathing and also during the daytime, most of us do not think about breathing as opposed to an ALS patient because we all know ALS patients eventually die because they cannot breathe, 95% of ALS patients die from lack of respiration. So, most of us do not think about breathing, but ALS patients are constantly thinking about, when am I going to lose my ability to breathe?

DR. BLOOM:

So, what goes wrong specifically in the breathing of ALS patients and take us sort of from the very beginning when it starts and to the end when they are no longer able to breathe at all?

DR. ONDERS:

In ALS, we know that patients are losing their motor neurons throughout from their initial diagnosis until their death. They lose anywhere of what we call the forced vital capacity of how much you are breathing about 1% to 3% of that forced vital capacity is lost every month. So, on most ALS patients you can almost graph them until they get 2 sets of low forced vital capacities if they need augmentative breathing techniques such as noninvasive positive-pressure ventilation also called BiPAP or invasive ventilation through a tracheostomy. As they lose those motor neurons, they lose their ability to breathe, both our accessory muscles, our ability to cough, and also our diaphragm. The diaphragm obviously is the key muscle for breathing because as we have seen in all of our spinal cord patients that we have implanted with the diaphragm pacing systems is that we can provide respiration just by the diaphragm alone. When we began this project on ALS our goal was actually just to help maintain the strength of the muscle that was left. Obviously, as we have been doing this trial up to 140 patients worldwide, we have actually identified a lot of other beneficial effects of what we call pacing the diaphragm.

DR. BLOOM:

So, how early in the ALS disease process do the breathing issues come up and typically how long is the actual course for the average patient?

DR. ONDERS:

Most patients with ALS from initial symptom presentation to actually death is anywhere between 3-5 years. Many times it takes a little while to diagnose the ALS, so can actually be a much shorter time period from diagnosis to death. What we know is that our breathing system is tremendous. Obviously, as you develop ALS, your ability to walk and move is less. So, your need for taking deep breath is less. What we find out though is that the patients are progressively losing their ability to breathe, but because we have such additional muscles, most of us require breathing only using 30% of our diaphragm for maintaining ventilation. So, you actually have to lose a fair amount of your ability to breathe before you actually have some symptoms. We have also seen patients that initially present with an elevated diaphragm on a chest x-ray may have lost with an idiopathic phrenic nerve paralysis 1 diaphragm. They may have just having occasionally may begetting short of breath and they have lost one full diaphragm function. Same thing with ALS patients. By the time we diagnose this, start doing studies, we found that many of them have lost up to 30% to 50% of their ability to have a ventilation so their forced vital capacity is already dropped down to 70% or 50% of the predicted values.

DR. BLOOM:

So, what treatments have been tried in the past and how successful were they?

DR. ONDERS:

The only FDA approved treatment for ALS is a drug called Rilutek, which out of the French studies lengthen life anywhere between 3 to 6 months. That is just lengthening lifetime. BiPAP where noninvasive positive pressure ventilation is used to augment the respiration, but we all know that using positive pressure ventilation or BiPAP is sometimes very difficult in patients with bulbar symptoms, 30% of ALS patients present with some bulbar symptoms where they have difficulty swallowing, difficulty talking, and that becomes much more difficult to tolerate the mask. Overall, BiPAP is only tolerated by anywhere between 10% to 40% of patient's. It's just difficult to tolerate that mask when you have ALS. BiPAP has been shown to help them ventilate and breathe for a longer period of time. Part of our research has shown recently though that a New England Journal Article that came out in March showed that just one night of being on positive pressure ventilation if your diaphragm is not working, you start converting for type 1 muscle, the slow twitch muscle fiber, to type 2B muscle fiber. So, we now have shown some evidence in our ALS patient populations that we are studying that their BiPAP actually does the same thing and actually weakens the diaphragm a little bit more. It has proven to be effective though, but as we know most ALS patients, once they start using some positive pressure ventilation, be it noninvasive or invasive ventilation, they become more and more dependent on it. That has really been the only therapy out there for ALS in this orphan disease.

DR. BLOOM:

And, for the patients that are on positive pressure oxygen, does that actually lengthen life and does it improve quality of life at all?

DR. ONDERS:

Positive pressure ventilation does improve the length of life. They also helps with the sleep dysfunction, something we have also shown with our researcher is that many of our ALS patients have developed central sleep apnea similar to the Ondine's curse that we see in children. Ondine being the ancient German mythological god that married river nymph and the other gods punished him that if he ever fell asleep with her, he would die. So, we know in that disease process is that of the preBotC complex is effective in those children and we have now identified in ALS that they will also develop central sleep apnea and so if they have a difficulty sleeping, we all know that BiPAP and noninvasive positive pressure ventilation works very well and helping those patients substantial sleep apnea. Diaphragm pacing, part of my research that we have been doing, we have now shown also very positively affects that by allowing natural diaphragm breathing at night, we no longer have the signals that fire and take a regular breath. So, these patients basically just stop breathing at night.

DR. BLOOM:

So, tell us about the diaphragm pacing system. What is it? How long has it been around and how are we using it?

DR. ONDERS:

Thank you, and I <_____> we began as whole system for spinal cord injured patients, obviously, a high tetraplegic patient, a C2 injury, has lost control of the diaphragm and we developed through Case Western Reserve and our Function Electrical Stimulation Group, a technique that I have been part of this process for over 10 years now where we actually implant electrodes on the diaphragm laparoscopically. That is how minimally invasive surgeon can <_____> what I do is laparoscopic surgery. So, we implant electrodes on the diaphragm after finding out the right spot for implanting these electrodes. We then stimulate the diaphragm and get a breath. What we found is that it actually worked extremely well in spinal cord injured patients. Our first successful patient and our first try was Christopher Reeves, Superman. We implanted him in 2003 and we actually got him off the ventilator until his untimely demise from other reasons. Our first patient, we ever implanted with a diaphragm pacing system was implanted in the year 2000 and he has been using our system for 8 straight years for every breath 12 times a minute, 24 hours a day. Several years ago, we began looking at another group of patients where I had a little interest in ALS, ALS being a different disease where they are losing motor neurons. We did not know if we could actually have a beneficial effect, so we initially began a pilot trial in 2004 and we have now just completed our long-

term pivotal trial in the United States for patients, which included 100 patients at websites such as John Hopkins, Mayo Clinic, Stanford, and several other sites around the United States along with several European sites and we are still looking at that data where we have shown in our initial pilot data and some of our earlier implanted data that we are having a significant effect on survival on patients with ALS by maintaining both those motor neurons and maintaining diaphragm strength.

DR. BLOOM:

So, who invented this treatment in the first place? Where did the idea come from?

DR. ONDERS:

I have actually been around with it since the beginning of it. What is very interesting is that it was developed by a group of engineers at Case and myself and the ALS project has really turned over completely to myself. My mentor was Tom Mortimer, a great electrical engineer at Case Western Reserve and he is kind of since his semi-retirement, has solved these great stressors. They never completely ever retire. A hump has been kind of helping to guide the project still but it resolved and really invented right here and we subsequently found that the company that actually provides the device also.

DR. BLOOM:

And when you were thinking about this, what prompted you to say, hey, I wonder if we can electrically stimulate the diaphragm to control breathing. When did those <_____>

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