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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

The Importance of the Patient Experience During the Treatment of Spinal Muscular Atrophy

ReachMD Announcer:
Welcome to ReachMD. This medical industry feature, titled "The Importance of the Patient Experience During the Treatment of Spinal Muscular Atrophy," is sponsored by Biogen. This program is intended for healthcare professionals and is *not* meant to provide medical or other advice; all treatment decisions should be made at the discretion of the healthcare provider and the patient, as each patient's situation may vary. And now, here's your host, Dr Charles Turck.

Dr. Turck:
This is ReachMD, and I'm Dr Charles Turck. Joining me to discuss the importance of the patient experience during the administration process for the treatment of spinal muscular atrophy, or SMA for short, are Dr Nassim Rad and Dr Kevin Koo. Dr Nassim Rad is a neuromuscular specialist in Seattle, WA, and Dr Kevin Koo is an interventional radiologist in Seattle, WA. Dr Rad and Dr Koo, thanks for being here today!

Dr. Rad:
Thank you for having me.

Dr. Koo:
It's a pleasure to be here.

Dr. Turck:
Before we begin, I'd like to disclose that all guests are receiving compensation from Biogen. So let's dive right in starting with you, Dr Rad. Why is it important to diagnose and treat patients with SMA as soon as possible?

Dr. Rad:
Long delays in diagnosis and treatment of SMA increase the risk of irreversible motor neuron loss and disability. As SMA progresses over time, motor neuron degeneration becomes unpredictable and less able to be reversed. This neuronal degeneration occurs throughout the life of individuals with SMA, even in adulthood, so it's imperative for patients to receive treatment that can preserve motor function for as long as possible.[1,2] Therefore, it is very important to educate our patients on how critical it is to obtain treatment. It is always more impactful to frame these conversations while taking into account the patients' values, goals, and knowledge base.[1,3]

Dr. Turck:
Turning to you now, Dr Koo, can you give us an overview of the SMA care team and the role of interventional radiologists, also known as IRs?

Dr. Koo:
Sure. Treatment of SMA requires a multidisciplinary approach. The care team might include a neurologist, nurse, radiologist, orthopedist, neurosurgeon, physical therapist, anesthesiologist, and pharmacist. But the care team can look very different for different patients, depending on their needs.[4,5] IRs are typically consulted to help determine an approach that maximizes the chance for a successful procedure. And so they need to be familiar with different techniques and complications of intrathecal drug administration.[5]

Best practices include collaboration and communication within the care team, because those are really important for patient outcomes and understanding patient needs. Not only do IRs work with the multidisciplinary care team, they also maintain good relationships with their patients to enhance patient satisfaction with their treatment.

Dr. Turck:
Before we continue, let's take a moment to review some important safety information.

ReachMD Announcer:
INDICATION
SPINRAZA® also known as nusinersen is indicated for the treatment of spinal muscular atrophy (or SMA) in pediatric and adult patients.[6]

IMPORTANT SAFETY INFORMATION
Coagulation abnormalities and thrombocytopenia, including acute severe thrombocytopenia, have been observed after administration of some antisense oligonucleotides. Patients may be at increased risk of bleeding complications. In the sham-controlled studies for patients with infantile-onset and later-onset SMA, 24 of 146 SPINRAZA-treated patients (or 16%) with high, normal, or unknown platelet count at baseline developed a platelet level below the lower limit of normal, compared to 10 of 72 sham-controlled patients (or 14%). Two SPINRAZA-treated patients developed platelet counts less than 50,000 cells per microliter, with the lowest level of 10,000 cells per microliter recorded on study day 28.

Dr. Turck:
With the important safety information in mind, let's take a closer look at how SPINRAZA is administered. Dr Koo, can you walk us through the SPINRAZA intrathecal injection process?

Dr. Koo:
Of course. SPINRAZA is administered intrathecally by, or under the direction of, healthcare professionals who are experienced in performing lumbar punctures, which directly delivers SPINRAZA to the cerebrospinal fluid, or CSF for short.[6] In clinical trials, SPINRAZA was studied using intrathecal administration via conventional lumbar puncture.[6]

The recommended dosage is 12 milligrams or 5 milliliters per administration,[6] and SPINRAZA treatment is initiated with 4 loading doses.[6] The first 3 loading doses should be administered at 14-day intervals, the fourth loading dose should be administered 30 days after the third dose, and a maintenance dose should be administered every 4 months thereafter. Please refer to section 2.1 Dosing in the USPI for further information on missed or delayed dosing. SPINRAZA has a long half-life in the spinal cord. In CSF, it's 135 to 177 days, and in plasma, it's 63 to 87 days.[6]

Following intrathecal administration, trough CSF concentrations of SPINRAZA were higher than the trough plasma concentrations.[6] Due to the risk of coagulation abnormalities, thrombocytopenia, and renal toxicity, you should conduct laboratory tests at baseline, before each dose of SPINRAZA, and as clinically needed.[6] Those tests include platelet count, prothrombin time, activated partial thromboplastin time, and quantitative spot urine protein testing.

ReachMD Announcer:
Renal toxicity, including potentially fatal glomerulonephritis, has been observed after administration of some antisense oligonucleotides. SPINRAZA is present in and excreted by the kidney. In the sham-controlled studies for patients with infantile-onset and later-onset SMA, 71 of 123 SPINRAZA-treated patients (or 58%) had elevated urine protein, compared to 22 of 65 sham-controlled patients (or 34%).[6]

Dr. Turck:
Now if we come back to you, Dr Rad, I'd like to switch gears and gain a better understanding about the injection process from the perspective of patients and their families. So during a SPINRAZA injection, what kind of impact can a patient's experience have on treatment satisfaction?

Dr. Rad:
This is such an important question, because a negative injection experience can greatly impact a patient's treatment satisfaction, and intrathecal administration can be particularly challenging for some patients with SMA. For instance, some patients may require the presence of some individuals from their multidisciplinary care team to help troubleshoot any issues with coordination of administration and they may recommend changes for their next injection. In addition, some patients may require sedation and radiation exposure, which can all cause concern for patients.[7]

Additionally, for patients with complicated spines, sometimes lumbar punctures are technically more challenging to perform and may not be successful at the first attempt. And so that can be a very negative experience for them.[7,8]

Dr. Turck:

With that in mind, Dr Rad, what steps can patients take to make sure they have all the information they need to prepare for their injection?

Dr. Rad:
So in general, patients are very proactive about seeking information on the injection experience. Many patients want to get both the medical and the patient opinion, so they go on social media to discuss their injection experiences and learn from what others have experienced as well. But we need to help patients understand that what they see on social media may differ from what they actually experience and that all patients experience different results. So communicating about the treatment and making sure they have all the accurate information they need to prepare for the injection can help manage patients' expectations.

Dr. Turck:
And Dr Koo, what concerns do your patients with SMA and their families have regarding the SPINRAZA administration process? And how do you navigate those conversations?

Dr. Koo:
Based on my experience, patients are often concerned about any discomfort they may feel and how long the procedure will last.[7] While lumbar puncture is a known medical procedure, side effects, such as headache, back pain, and transient or persistent cerebrospinal fluid leakage, have been documented. And so we discuss this with patients and their families.[8,9] Additionally, many patients come to the clinic after driving long distances, so it's an important day for them. We encourage them by saying that this day is about them and that we will try to find a position that works for them. And so our overall goal is to try to make sure they feel comfortable in the clinic to enhance patient satisfaction.[7]

Dr. Turck:
And after you address the concerns of patients with SMA and their families, Dr Koo, how do you go about planning for a SPINRAZA injection in an adult with SMA?

Dr. Koo:
Well first, I think it's important to note that administration of SPINRAZA may be complicated in some patients, and so their frailty and special needs must be considered when administering medications intrathecally. I consider sedation as indicated by the clinical condition of the patient and consider ultrasound or other imaging techniques to guide intrathecal administration of SPINRAZA, particularly in younger patients. Some other special considerations might include patient size, including patients that are small or overweight, spinal complications such as scoliosis, or corrections for spinal complications like implanted rods or spinal fusion.

Patients can have contractures that limit movement and mobility, which can make positioning challenging. They can have weakened respiratory muscles that result in decreased lung capacity and expiratory flow. They can also have impaired cough function or increased risk of infection. And so all of these considerations need to be weighed when thinking about a treatment plan for your patients.[4,8,10-13] For some of these considerations, I order a computed tomography (or CT) scan before getting started. This allows me to gain a sense of what technique I'm going to use during the procedure, as well as to come up with a plan B.

ReachMD Announcer:
Laboratory testing and monitoring to assess safety should be conducted. Perform a platelet count, coagulation laboratory testing, and quantitative spot urine protein testing at baseline and prior to each dose of SPINRAZA and as clinically needed.[6] Severe hyponatremia was reported in an infant treated with SPINRAZA requiring salt supplementation for 14 months. Cases of rash were reported in patients treated with SPINRAZA. SPINRAZA may cause a reduction in growth as measured by height when administered to infants, as suggested by observations from the controlled study. It is unknown whether any effect of SPINRAZA on growth would be reversible with cessation of treatment.

Dr. Turck:
And what are your next steps, Dr Koo, after you consider all those factors?

Dr. Koo:
When the neurology team decides to treat a patient with SPINRAZA, the neurology, neuroradiology, and interventional radiology departments need to reach a joint decision regarding which of them will administer SPINRAZA, based on the patient's history, age, anatomy, and spinal imaging. The team also discusses if anesthesia is needed based on a patient's respiratory baseline.[5,14] Now positioning a patient with SMA for a lumbar puncture can be challenging, due to some of the factors outlined previously. Because of this, it's important to consider methods that may help patients feel comfortable during the procedure.[8,12] For instance, ultrasound or other imaging techniques like fluoroscopy and CT can help guide intrathecal administration.[6,8,11,12] Pre-procedure X-rays may also be

required to determine spine clearance, and this should be considered before a procedure is planned.[12]

Now with all this being said, intrathecal injections in patients with complicated spinal access often require technical adjustments, an altered injection approach, and additional resources, but it is possible to intrathecally administer SPINRAZA using the standard or conventional lumbar puncture, interlaminar lumbar puncture, and transforaminal lumbar puncture techniques.[8,15,16]

Dr. Turck:
And Dr Rad, in what ways can neurologists and IRs help their patients prepare for a SPINRAZA injection?

Dr. Rad:
So neuromuscular specialists and IRs typically set patient expectations by discussing all aspects of the SPINRAZA injection. For example:

We discuss what tests and assessments to expect before the administration. Labs may be needed days ahead of time to clear a patient for treatment, or they may be done the same day as the procedure. The injecting physician will review platelet counts and prothrombin time for safety of intrathecal injection. Motor function assessments are also conducted by the prescriber days beforehand to monitor patients response to the treatment.[6]

We then discuss what to expect on the day of SPINRAZA administration; we remind the patient that SPINRAZA is administered as an intrathecal injection using a specialized spinal needle and is injected over 1 to 3 minutes. Before we begin administrating SPINRAZA, we remove 5 milliliters of CSF, and we decide together which position is right for the patient. Imaging and sedation may be used to help facilitate the intrathecal injection. We talk through the patient's concerns about the spinal tap, like the pain associated with the procedure, and we also do the best we can to make the administration as comfortable as possible. [6,12,17] Lastly, we then prepare our patients for what to expect post-procedure and discuss the adverse events associated with SPINRAZA treatment.

ReachMD Announcer:
The most common adverse reactions (≥20% or more of SPINRAZA-treated patients and ≥5% more frequently than in control patients) that occurred in the infantile-onset controlled study were lower respiratory infection and constipation. Serious adverse reactions of atelectasis were more frequent in SPINRAZA-treated patients (18%) than in control patients (10%). Because patients in this controlled study were infants, adverse reactions that are verbally reported could not be assessed. The most common adverse reactions that occurred in the later-onset controlled study were pyrexia, headache, vomiting, and back pain. Post-lumbar puncture syndrome has also been observed after the administration of SPINRAZA.[6]

Dr. Turck:
Well, we've certainly covered a lot of ground today, but before we close, I'd like to open up the floor to each of you. Starting with you, Dr Koo, what impact can this type of support have on patients and their families?

Dr. Koo:
So everything we've discussed today is set up to help patients plan for their injection day and facilitate the process for SPINRAZA administration in an appropriate setting per institutional care guidelines. But what's just as important is post-administration monitoring and ensuring that appointments are also scheduled for continued loading and maintenance doses.

Dr. Turck:
Thanks, Dr. Koo. And Dr. Rad, I'll give you the final word.

Dr. Rad:
When we perform this procedure, it's critical to monitor the patient's safety, for example, when difficulty with airway management or sudden changes associated with procedures and sedation occur.[18] And so an organized approach and team planning framework are key to the execution of treatment plans and attaining optimal SPINRAZA dosing workflow.[14]

Dr. Turck:
Well with those final thoughts in mind, I'd like to thank my guests, Dr Koo and Dr Rad, for joining me today to share their own experiences with the SPINRAZA administration process. Dr Koo and Dr Rad, it was a pleasure speaking with both of you today!

Dr. Koo:
It was great to be here.

Dr. Rad:
Thank you. It was a pleasure.

ReachMD Announcer:
This program was brought to you by Biogen. To revisit any part of this discussion, visit ReachMD.com/IndustryFeature. In addition, for more educational videos about SPINRAZA, please visit SPINRAZAhcp.com

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