# Adult Considerations in Spinal Muscular Atrophy: Building Clinician and Patient Medical Teams

# CMEO Podcast Transcript

**Claudia Chiriboga:**

Hello. On behalf of CME Outfitters, I would like to welcome you to today's educational activity titled "Adult Considerations in Spinal Muscular Atrophy: Building Clinician and Patient Medical Teams." Today's program is supported by an educational grant from Genentech, a member of the Roche Group. And brought to you by CME Outfitters, an award-winning accredited provider of continuing education for clinicians worldwide. My name is Claudia Chiriboga. I'm a professor of neurology and pediatrics with the division of Pediatric Neurology at Columbia University Medical Center, New York, New York. And today I am delighted to be joined by two panel members who will introduce themselves.

**Vanessa Battista:**

Thank you, Dr. Chiriboga. I'm Vanessa Battista, I'm a pediatric nurse practitioner and I'm currently the senior nursing director of palliative care at the Dana-Farber Cancer Institute in Boston, Massachusetts.

**Claudia Chiriboga:**

Welcome, Vanessa.

**Vanessa Battista:**

Thank you.

**Tina Duong:**

Hi everyone. My name is Tina Duong. I'm a physical therapist at Stanford University and I direct the clinical outcomes and research development in our neuromuscular division.

**Claudia Chiriboga:**

Welcome, Tina. Very well, let's get started. Our learning objectives are threefold. One is to assess the burden of SMA in adult patients in a wide range of areas. And to develop best practice interdisciplinary strategies for transitioning patients from pediatric to adult care. And to integrate proper therapeutic approaches for the care of the adult patient with SMA. So, what we'll do now is the survey, and if you would answer, what is the driving force behind the increased quantity of adult patients with SMA in recent years? We'll wait for your answers. Okay, most of you answered the advent of disease-modifying therapies, which I think is a really good response. Moving forward. Tina, why don't you share with us some of the background of SMA and its phenotypes?

**Tina Duong:**

Great, thank you so much, Dr. Chiriboga. I'll give you the basic natural history of this SMA phenotypes, which is changing and dynamic. And so, historically speaking, we classified SMA from non-sitters, sitters, and walkers functionally. And based on the genotype and the presentation, we described patients as type 1, 2, 3, or 4. As you can see here, 60% of patients are typically type 1 individuals who are non-sitters or the presentation was presented at birth. What that means is they were never able to sit up independently, hold their head up, or move really their limbs against gravity. And so they usually have respiratory failure that results in mortality around the age of two. Those who are considered classification of SMA type 2, which is 20 to 30% of the population, they don't independently walk, but they're able to attain sitting. And usually have a survival rate of around 25 years of age.

Those who are typically described as SMA type 3, which is 10 to 20% of the population, means that they attain ambulation. And so they may have some delayed motor milestones but attain the ability to walk. However, there's a variability in the timing of when they lose that ambulation. They usually have a normal life expectancy, but something to consider is that beyond having SMA is a decreased activity or physical activity in their lifestyle. So, some of the increased mortality related to deconditioning and sedentary lifestyle may contribute to, I think, a lower mortality than if you looked at those who were more physically active there.

Then the type 4, it's generally more rare. And they retained the ability to walk and "has a more normal life expectancy" and usually diagnosed at a later stage in disease. But they still have some decreased muscle strength and progressive loss of muscle strength throughout the lifespan. Okay.

When we're looking at advances in SMA management, many of you are here because you're wanting to look at and learn about what the changes in disease management is going to impact how you clinically practice. So, in doing so, my colleagues will talk to you about how that may impact the various components of care, but we really have to historically look at what that means. If you look at SMA and the gene was, the causative gene was discovered in 1995. And it wasn't until 2007 that we first published the standards of care. And in this first publication of standards of care, what it really did change was the respiratory management of these patients, which really prolonged the life expectancy of these patients because of standards of care management. Then, as you can see, in 2016 it was a pivotal moment in December that I don't think any of us would ever forget was when nusinersen, the first disease-modifying treatment was approved.

As you can see here, there's this 2017, the second standards of care was published. But keep in mind, the second standards of care was published and thought about with meetings prior to the actual treatment being approved in 2016. So, many of the standards of care that was suggested then was based on clinical expertise. That was really based on a normative population that wasn't based on disease-modifying treatment. As you can guess, we anticipate an updated standards of care, but in the moment we're in this dynamic process of understanding what is the impact of disease-modifying treatment. And then as you can see in 2019 and 2020, we have the approval of gene therapy in 2019 and risdiplam in 2020. When we're looking at adult care, the most prevalent and disease-modifying treatment for our patients would be the approval of nusinersen and risdiplam.

**Tina Duong:**

One of the things when we look at adult challenges is that the studies in the clinical trials that have medical impact and that we're looking at interpretation and access to treatment has a lot to do with the clinical trials. And many of the clinical trials are related to pediatric studies and pediatric-related outcomes. However, numerous studies have been published since then worldwide indicating that for adults with chronic SMA there are other organ systems that may be impacted. And that includes bulbar weakness including speech, swallowing, nutritional status, and the ability to communicate. This implies and is impacted on quality of life. Other gross-motor and fine-motor activities that we're seeing is not typical to some of the Hammersmith Scales that you may see are associated with the ability to move more distal movements such as head movements or fine-motor movements that may not be seen in some of the typical scales in SMA of the Hammersmith or the RULM.

And so as we're learning and seeing how this is impacted, we're realizing that some of these scales have gaps that we need to measure outside of the clinical trials. Beyond the motor assessments, we're really also looking at pain and fatigue that is not really well differentiated or characterized for these patients. We have fatigue that may be cognitively reported, but also physiological fatigue that's associated with muscle-related fatigue that we're not able to quantify. So, those are some of the things that have shown to possibly be improved in patients who have disease-modifying treatments that we're not seeing, that's not being seen in the typical outcome motor scales in the clinical trials. Beyond that, we know that patients with longer duration of disease also are impacted by respiratory weakness, and that includes impaired or decreased fatigue, impaired cognition, sleep disturbances, and lung infections. As you can see here, the PROMIS fatigue scale shows the T-Score of typical individuals reporting fatigue. And you can see here on the left with the pink bars that those who normally have about a T-Score of 50, those with individuals have much greater fatigue that's associated with SMA.

And that's something that should be addressed in the clinic and has a great impact for our patients. Because even though there may be not functional clinically related measures that are changing, but the endurance aspect of some of these disease-modifying treatments are impactful. When we ask patients about patient-reported outcomes that are impacted by the symptoms of adult SMA, some of the quality-of-life assessments, as you can imagine, were related to the motor outcomes. Related to their ability to walk, the ability to do activities of daily living, for example. However, some of the impacts that I think are gaps in our ability to measure are fatigue and distal hand motions that are associated more so with adult chronic disease. And so that includes also pain, gastrointestinal issues and disturbances in sleep.

And so those are some of the things that have increased prevalence. And this compounds when it comes to the impact of not only SMA but the longer duration of having a disease, the decreased deconditioning of not having physical activity, and on top of it aging. And so a lot of these patients who are not moving, they have limitations not only in mobility, posture, respiratory and Bulbar function, but they have orthopedic difficulties including hip dislocation, subluxation, and scoliosis and contractures due to the compounding muscle imbalances seen with the chronic aspect of this care, of SMA.

**Tina Duong:**

One of the things that we really like to highlight is the differences in SMA management in regards to children versus adults. Typically, the standards of care suggest a multidisciplinary approach. And when the model, especially in the US there's a multidisciplinary care team in which the patients come into the clinic and they're able to see a lot of disciplines, including all those that impact multiple organs. We know that SMA impacts not only muscle but respiratory cognition that requires care that's focused on social work, respiratory care, physical therapy, occupational therapy, speech language pathologist. The nice thing about the pediatric clinic, typically the care focus is driven by the patient or the patient's family. And it is coordinated by a team and most of the time the nurse practitioner. I mean, the responsibilities on the patient is pretty low because they're children. And the priorities typically are about physical health and motor milestone development. Some of the supportive services that we also talk about and collaborate with are the school systems.

However, the stressors really rely on the caregivers themselves. However, when you transition to the adult clinical care team, not only is that transition, as Vanessa will talk about a little bit later, it's not coordinated. But now all of a sudden we come from indirect management of care from the patient being managed by a say nurse coordinator themselves, it becomes a responsibility of the adult patient. And on top of it there's very minimal institutions that have a multidisciplinary approach where they have all the disciplinary themes in one visit. And so the patients themselves have to make these visits themselves. And they have a very fragmented care pathway. And the responsibility really entirely lies on the patient to be able to access the care and get the appropriate access to gain all of these preventative measures.

**Claudia Chiriboga:**

Thank you, Tina. Let's move on to the discussion. I wanted to ask you, Tina, I saw that PROMIS that it looks like a lot, but it was less than one standard deviation because it was like seven, eight, and 10, which doesn't look like it's large enough for the fatigue that I'm used to seeing. Do you find a differential in fatigue, and at least I think I do, when you have your ambulatory patients who are at work, walking all day, that they suffer a lot more fatigue than the patient who's in the wheelchair who's able to manage a little better because they don't have that type of exertion. Is that your experience as well?

**Tina Duong:**

I think it's all relative, right? Because for the patients who are walking, they're walking possibly more. But the patients who are non-ambulatory, they're sitting upright. And sometimes sitting upright causes the same amount of fatigue based on the muscle function that they have or the ability to, for example, a patient who can spend all day using the mouse when before they could not do that. Or be able to move their finger all day and stay at a eight-hour work week when they needed an assistance to help move their finger on the mouse previously. So, I think it's all relative in regards to fatigue. But fatigue I think becomes more of a factor on the adult chronic SMA stage compared to the pediatric. Or maybe in the pediatric stage the kids don't verbalize it as well.

 

**Claudia Chiriboga:**

Okay. Yeah, all right. Very good. And what can you do to prevent the contractures? I mean, the little ones get out and they're moved around a bit more, but it's so hard to get wheelchairs, insurance to approve standing wheelchairs, extension of the legs. What can our adult patients do to help minimize that contractures from sitting all day at work or at school?

**Tina Duong:**

And so because of the muscle weakness and the imbalances, a lot of times it has to do with positioning. Stretching itself, the literature doesn't show that stretching will improve range of motion. It does improve tightness so that you have the ability to move. However, I think the important thing for adults in the saving of time and efficiency is to make sure that you're positioned really well, and throughout the day changing the position to ensure that your joints go through that range or that passive range so that it's not always in a static position.

**Claudia Chiriboga:**

Excellent, thank you. We're running short of time. So, why don't we go to this next survey. And this is more subjective than the last question. How confident do you feel in your ability to contribute to a smooth adult care transition for youth and young adults with SMA? Okay, well, nobody's suffering from hubris. So, hopefully with time everybody will feel a little better, but I think maybe we'll have a better idea once we hear from Vanessa about what's the best approach to maneuver this transition. Vanessa?

**Vanessa Battista:**

Thank you, Dr. Chiriboga. I would, oops. Okay. Oh, I just want to share with you to start some of the experiences that patients have shared with us about their process of care transition. These are direct quotes on the slide here. You can read some of them and I'll just share a couple of them with you. So one person said in our survey, "Going from a children's hospital where they explain everything in great detail to the adult healthcare environment where they expect you to know the majority of things, you pretty much had to be on the ball all of the time." And someone else said, "I've encountered countless barriers transitioning to adult care, like getting insurance to approve therapy for me. At the time when I was diagnosed my mom was my advocate. She was very strict, very firm, and she did what she could. My care team helped educate her. As I became an adult, I had to take over the advocating role in my own life."

So, this just gives us a glimpse into what the experience is as we prepare for a transition with the individuals and families that we work with. I want to talk now a little bit about some of the specific gaps and barriers that we experience as part of the transition process. And it's important to be mindful of the fact that the gaps and the barriers or some of the challenges exist for both the patient or the individual living with SMA and their family, as well as for clinicians. So, patients have specific needs during care transition and there's a lot of anxiety with this process. There's anxiety regarding the transition over from pediatric care to adult care. And it's very normal to experience this kind of anxiety.

**Vanessa Battista:**

For many of these families they've been cared for in one place for a very long time, right? We've gotten to know them quite well as their care team and suddenly they're switching over to a new team of people that they don't know yet. If you're a family watching this now you may be familiar with that where you're experiencing this, where suddenly it feels like this huge shift, there's anxiety around that. There's maybe fear that your expertise won't be valued as the family becomes the expert, be very well known, and perhaps suddenly with a shift they may not know you and know as much about how much information you have. And that there may be some relinquishing of responsibility there. And as a parent that can be very anxiety-provoking when you've been doing this for many years. Another challenge can be inadequate planning. Someone might be unfamiliar with the responsibilities that come with transition.

We often say that transition is not one point in time. Transition is a process that should take place over a period of time. And so there needs to be a lot of planning that comes with that. And sometimes there's not really a process if there aren't the people to do it. As Dr. Duong just mentioned before that usually there's point person on the team, but there really is a whole process involved. There also may be more of a focus on psychosocial engagement. When you're younger, then there is in medical care, and suddenly when you transition into becoming an adult, as we just heard in that last quote, you are expected to be your own advocate, to know your own information. And when we are going through this process of transition, that's one of the ways to assess readiness is to make sure that someone can answer all of those questions.

Do you know who your insurance provider is? Do you know the medications you're taking? Do you know who to contact for an emergency? Things like that. So there really needs to be some readiness there. There may also be difficulties with the system. Limited clinician availability. It's harder to find adult providers. And now fortunately there are more and more people living with SMA into adulthood, but we haven't necessarily always been prepared for that. Because these treatments are new and people are living longer and which is an awesome thing. But we need more and more clinicians trained to be able to care for this population. So, there may be difficulties in finding a provider who can provide this care and also services to meet the needs of patients. There may also be a lack of medical records transfer, so it can be difficult sometimes to get all the records and all of the information transferred over.

There may also be insurance coverage gaps as there's a transition from pediatric to adult care. And you want to also make sure that the adult providers take the same insurance that their insurance will carry over for adult care as well. There may also be transportation limitations. I can think of a time when we had a patient who literally their van, their accessible van would not fit into the entrance to the adult hospital and it always fit into the entrance in the pediatric hospital. So, just things to think about, these little logistics of how will this happen. Some of the barriers for clinicians are communication or consultation gaps between the former, the pediatric health care providers and the new team just having an opportunity to do that. And between the adult specialist, as Dr. Duong also mentioned, for pediatrics it's often all in one place, but in the adult world the care may not be happening altogether.

 

**Vanessa Battista:**

For example, physical therapy, occupational therapy, all of your specialist nutrition may not all be at one clinic appointment, so the communication can be fragmented more so in the adult world. There may also be training limitations, lack of knowledge on adult care for people with SMA, because the guidelines have always been based on pediatric care or more so based on pediatric care. There may be support gaps for a family when there's unfamiliarity with care needs or local support services for young adults. There may also be a lack of mental health resources that may be important during this time, especially if there's anxiety around this transition. There may be administrative constraints, insurance, which I talked a little bit about the insurance coverage gaps, the lack of time and reimbursement and lack of electronic health record that can carry the records over from the pediatric provider to the adult provider, as well as a lack of patient engagement.

When a family is feeling anxious they may not be as engaged or as willing to meet with the adult team. And so there is lots of support that's needed around this process and it involves being very proactive and navigating the system and helping guide families through that. So, let's talk now a little bit about some of the strategies for improving the transition and care transition. So, the responsibilities lie both with the individual living with SMA and their family, as well as with the team. But I want to talk a little bit about what the responsibilities are for the patient. So first there is a need to develop and apply new coping skills, to increase the sense of autonomy and self-agency. Again, that was mentioned that piece about being an advocate for oneself, to renegotiate relationships with adults. And this can be a really big shift in pediatrics.

The parents are often in the room or the guardians for every single visit. They have a very active role. And suddenly if you transition over to the adult world, it may not be the same expectation. You'll also need to meet the demands of increasingly mature roles. And again, be your own advocate and be responsible for your own material. And then take responsibility for medical tasks as well. Along with these responsibilities for the patient and the family are the responsibilities of the care team, which are really great responsibilities and something that needs to be taken very seriously. There needs to be a proactive multidisciplinary collaboration, starting with planning transition. And there are guidelines around this, but some say as young as 12 years of age, we usually start around 16, 15 or 16. You want to ensure care continuity and use digital tools. There are some things that are being developed now, as well, there are resources available for families, but things like telehealth apps that may be very helpful to keep track of things.

You also want to think about helping families foster autonomy, teaching self-advocacy, providing mobility or communication aids, more independence--in-home exercises as Dr. Duong also talked about, planning for insurance coverage. So, lots of different things to be mindful of. And again, this goes along with assessing readiness to transition. We want to make sure that all of these needs have been addressed before we successfully transition someone. As well as addressing the mental health and psychosocial needs that come along with this period of time. I think that that's all. And we can move on to some discussion here, Dr. Chiriboga. Thank you.

 

**Claudia Chiriboga:**

Okay. I don't have access to the slides. Can you move it forward? I'm not sure. Okay. So, Vanessa, you've brought up some very wonderful points, and, in an ideal world, all of those things would take place. But in many areas, there's not that kind of support for the transition. And some of the areas of concern are that there really isn't a designated SMA champion in the adult world. It has to start to be developed because there's more and more pediatric patients who will transition and become adults because they are surviving and they are stronger and active members of society. The other thing that many of the adult programs haven't really taken on as much as they should is the points that need to be done in order for insurance to approve. Many of them don't have the resources for the functional motor scales that many insurances ask for. Or the amount of labor and pre-authorization and letters of medical necessity that are needed to get started with medication. What kind of suggestions do you have that would help improve this type of issue that what happens with transition?

**Vanessa Battista:**

Yeah, so that's an excellent question. You brought up some really important points that first of all, there is the challenge of not having the same resources available to everyone. And I think this is sort of a bigger problem that unfortunately you can't fix instantly where some institutions or some medical centers just have a more robust team and offer more services and allow families to have a smoother transition. And of course, everybody deserves the same amount of support. But we know that the reality is there are places where there are more resources than there are in others. I think it's very helpful to try and identify a point person. On many teams it is a social worker who helps with this. It is often a nurse or a nurse practitioner, as Dr. Duong also mentioned. Sometimes obviously the physician or neurologist may also be involved with some of those letters.

But if there's a coordinator in clinic or which who may be a nurse or a social worker, it's helpful to have one person who really takes the lead on this and develops a process so that every time they're not repeating this for each family individually, that there is a smooth process. I think one thing that I've also found to be very helpful is having an identified point person to work with on the adult team. And again, this can vary from location, but in places where there are large centers, you may know the adult team very well and the majority of the patients may go to that one center. And so I know we've had experiences where I've worked where we have made it a point to reach out to the team there and for example, our social worker would connect with their social worker, our nurse or myself as the nurse practitioner would connect with the nurse or nurse practitioner there to ensure a smooth process.

But the things like insurance will always be a challenge. Writing the letters of medical necessity, all of those things remain a challenge. I think the thing we can do is anticipate the challenge and try and be prepared for it. So, if we know they're going to be needing certain letters, we prepare them in advance, we prepare a whole packet, we ask the adult team what is it that you will need so that for every patient we transition over, we can get everything together. Have they discussed goals of care, advanced care planning, things like that. We want to send everything with them.

**Claudia Chiriboga:**

Excellent. Thank you so much. We have a few questions. There's one on efficacy that I'll address during my piece, but there's something about if the patient stays on the parent's insurance to age 26, do you wait for a transition? And they're separate issues that the insurance will be there, but you do need to transition, because many places will not continue to see patients who are outside of the pediatric age range. That can be 18 or it can be 22, some a little bit more, but at some point, they will need to transition. And the multidisciplinary clinics typically do not want, the pediatric ones do not want to necessarily continue seeing patients that are adults and would like to transition them. Sometimes they have no choice if there's no one on the receiving end, but in some places, you cannot continue to see them past a certain age or pediatric hospitals don't have adult capacity. So it's best that they transition. And even if you do keep a patient, that patient will, if they have an issue, will need to be admitted to the adult hospital, not to a pediatric hospital.

**Tina Duong:**

I think one of the questions too is in regards to transitional care is that when we look at it longitudinally, we're comparing these motor outcome measures that payers are requesting such as the Hammersmith or the RULM scale. And how do you get that information from a pediatric clinic to the adult clinic being that in the US system or medical information system that varies. Depending on who your payer is or where you go, right? And I think some of the things that you said, Dr. Battista is about in regards to the transition is the anxiety that we can't emphasize enough from the adult perspective is the expectations. Management of expectation in regards to access and maintenance of care. Because of the clinical trials being in pediatrics, payer sources may change on their viewpoints of when they continue payments or continue treatment or start treatment.

So I think what I'm hearing from a lot of our adult patients is they have incredible amounts of anxiety based on coming to see someone like myself doing these physical therapy outcome assessments that may not necessarily be relevant to what they're able to do, but that's required by the payer authorities. And so I would really highly advocate for those who are on the line is that even though there are clinical outcome assessments that are typically used in outcome in the clinical trials. As clinicians, we know there are other outcome measures that may be more applicable to our individual patients and highly encourage that you continue to use your clinical expertise to utilize these assessments so that we could document changes that's outside of what's seen in the clinical trials.

**Claudia Chiriboga:**

That is a good point, Tina, especially for the type two's where MFM and RULM probably are better than the Hammersmith in terms of identifying changes. But also as clinicians documenting things that are not easy to assess with these instruments. And just reporting everything that the patient is discussing. And sometimes it has to do with infections, or breathing, or coughing, or articulation, support of the back and ability to type and do other things that are important for activities of daily living. All of that needs to be documented to build a case to be able to maintain treatment.

 

**Claudia Chiriboga:**

I think due to time, let's see if this is now working, let's talk a little bit about SMA multidisciplinary care and what all our roles are. This little graph shows the neurologist at the center along with a coordinator, but that sometimes can be a physiatrist, and then the various subspecialties that are helpful. Not all centers have all of these. The core might be pulmonary neuromuscular, of course, neurology and psychosocial are all possible. But some places have everything. But the places who don't have everyone there in clinic have identified champions that you can refer to for orthopedic issues or GI issues and the like. But from the neurologist's perspective, one of the main roles that we have now since the advent of disease-modifying therapies is to treat patients with SMA with these new modalities.

So, let's talk a little bit about what our options are in the adult SMA arena. We have nusinersen, it's an antisense oligonucleotide, has to be delivered intrathecally because it does not cross the blood-brain barrier. And what it does, it's an mRNA-splicing modifier that increases the amount of exon 7 that is transcribed from the SMN2 gene, thus producing more SMN protein, which is the main goal. And its dosing. There's a loading dose of four doses over two months, day 1, 15, 30, and 60. And after that that's every four months in perpetuity as long as the patient decides to continue treatment.

So the studies, and I think someone mentioned before, some of the nusinersen trials were all pediatrics. The oldest patient in the late-onset SMA was nine. And that study was supposed to go up to 12. So, there have been no adult placebo control trials with nusinersen. But there are two large observational studies, one by Hagenacker, and there was 139 patients. And as you can see, the median change in baseline on the Hammersmith over time was 1.7, 2.5, and 3.1 points. Now, if you look at this from the percentage of individuals who increased by three points, it's a lot more substantial. It's like 20 something, 30, and up to 40. These patients also showed improvement in ambulation. The majority of patients, about 60% were type three, and most of them were strong. The mean was I think about 300 meters. These were strong ambulatory patients who had a nice response and I think it was at 10 months, maybe 40-something meters walked. But again, it's not your typical patient population.

The Maggi is retrospective into 14 months and had a similar improvement of the Hammersmith over time. And the side effects were nausea, headache, fever, infection, and backache because of the procedure. And of course, when you have hardware, you need neuroradiology with fluoroscopy or foraminal injection, the SCT scan in order to administer it because you can't just do it blind the way we do in the younger children.

The next medication that's available is risdiplam and it's a small molecule given orally once a day and it also targets mRNA. It is also a splicing modifier similar to nusinersen, though it acts in a slightly different region on exon and intron instead of just intron 7. It can be given via G-tube or orally. And it's weight-based.

 

**Claudia Chiriboga:**

And there is a placebo control pivotal trial called SUNFISH. And it was two part, the first part was dose finding and the second part which had 180 patients and included patients from age 2 to 25 years of age found as the main outcome being the MFM 32 that over time there was a significant increase in the MFM at 12 months, and that's when the placebo ended and everybody started to be on the medication. But over time someone had asked, "Are there two-year data on risdiplam?" And here you can see that the response is sustained. And the response was seen also on the upper limb module. And the Hammersmith didn't have a response at 12 months, but by 24 months they were starting to see improvement as well. The JEWELFISH study, which is listed below, is more real world. These are patients that are much more heterogeneous, much wider age and have more chronic disease. Most of them have scoliosis. About a third of them have severe scoliosis and contractures.

And in this group, as you'd expect there was stability. They were able to maintain their function. And the most common adverse effects are fever, diarrhea, rash, oral ulcers or arthralgia, UTI. And as you know, there is a theoretical risk that it might compromise male fertility. And so there's a warning with regards to that. So, the question is, what are the treatment expectations? And just to review very briefly, this is taken from Kathy Swoboda's 2005 paper showing the decline in the MUNE, which are the motor unit number estimation that reflects motor neuron pools. And you can see that there's a rapid decline shortly after presentation. Much more severe in the type 1, less severe the slope in the type 2 and a bit more shallow with the type 3 and then a period of a pseudoplateau where it declines, but it's much more gradual over time. And that is reflective of the motor function that we see over time.

So, treatment response is much better when you treat early in the disease, like at the beginning when you have that acute phase where you've just started to lose function and there are motor neurons that can be recovered but haven't been lost completely. If you treat very late with chronic changes in advanced SMA, then you're not only going to have a much more limited pool of motor neurons that are able to be recovered, but you also have contractures and other changes that will limit any response that you have. So, it's the expectation of some improvement if you're younger or earlier in your disease course. And obviously stability would be a very good response for those who have more advanced chronic disease. Just keeping the function you have and not losing it would be an expectation.

And that is based not only on age, its duration, how long have you had the disease? And what stage of disease you were in for that period of time? For example, a 25-year-old non-ambulatory type three that just stopped walking is expected to have a much better response than 25-year-old type 2 who's been in a wheelchair since 18 months. And it would be stability that we look for.

Okay, so how do we optimize care for adults with SMA? And my question would be to the group, Vanessa and Tina, do you feel that adults, and maybe, Tina because you see more adults, if the adults that you're seeing in clinic have an understanding of the role of these medications or are they still not convinced that these are medications that might be beneficial to them?

 

**Tina Duong:**

I think it varies. I think we're seeing a lot more adult patients, because they are aware of treatment being available. I think the most prevalent questions we have is, how would that impact them? Because it's hard to interpret with the pediatric data. We do spend a lot of time trying to be very objective in the overview of the available information, including the adverse events. I think some of the things that we don't talk about as much on the pediatric side that is very significant on the adult population are adverse events. I find that most of the questions surround adverse events. I think the adult patients are very realistic. They're minimal expectations really come along the lines of expecting stabilization. They don't expect to jump out of their wheelchair or anything in regards to improvement in function. I think some of it is just like stabilization, improvement, endurance. But the biggest concerns are the adverse events. Because these studies were done in pediatrics, how do the adverse events relate to them and in their ability for future planning and especially in regards to some of the fertility reported adverse events from the risk plan treatment.

**Claudia Chiriboga:**

Okay. Vanessa, do you have anything that you'd like to add?

**Vanessa Battista:**

I think I just really would add that, again along with what we were talking about earlier, that this is really a process and that all of the pieces need to be considered. So, I appreciate the comments that Dr. Duong has made about the different measures that are needed. And I think it really brings up the point that part of the responsibility is on the patient and the family that we've talked about, and part of it is on us as health care providers. And I also think there's a need for us to work on changing this in the system and how we do this systematically. Because this is not something that's going to go away. There is going to be more and more and more of a need for this to successfully transition patients into adult care, which is a really great problem to have. But we need to make this easier so that every single time we do this, we're not reinventing the wheel, so to speak.

We're struggling for this to be difficult to try and get the measures that are needed to help families feel ready. So, I think it really is a process that involves a lot of people and a lot of different systems and really needs a process that's well established for this to work well over time.

**Claudia Chiriboga:**

One of the issues that I find problematic of is that in distinction too in the pediatric world where the educational system assists with the therapies, once our patients either start college or go into the workforce, the time or ability to have physical therapy on a regular basis is much more limited. And are there any strategies that either of you have that could be helpful in that regard to improve? Because again, these are individuals who are sitting all time, most of the time and that are not so light that they can just move, they need help for mobilization. So, lying down and sitting up is sometimes not that easy to come by, so they tend to spend a lot of time sitting, to minimize some of the contracture and the issues that we were talking about earlier.

 

**Tina Duong:**

Yeah, I honestly think that part of it is that it's a paradigm shift from this thought of we're just trying to decrease progression or maintenance to, we may improve. But none of us jump out of bed and become athletes. And so it has to be a slow process and an individualized exercise program that has to be initiated. I think part of it is some of the patients don't know what's safe. Because the information out there is pretty sparse and variable. And so one is that fear of implementing a physical activity or physical therapy program and how to do that in regards to access to physical therapy and what are the other alternative mechanisms to do that if you don't have physical therapy all the time. How can you have a home exercise program with a physical trainer or other people can help assist when you can't do some of these programs independently?

But the other piece is the individualized part of it is that they have to be in contact with someone that can guide them through the process. For one, it has to be safe. We really have to view exercise as a dosing mechanism. How do we dose exercise for patients to feel one, safe, and what is the appropriate dose for each patient from an individual perspective? The same dose is not applicable across non-sitters, sitters, and walkers. And so how do we make this to where it's relevant to them? And the idea is not for exercise, it's really to maintain an active lifestyle throughout their lifespan. And so that has to be in combination with adaptive or assistive technology so that patients can do things that makes them happy and brings them joy.

**Claudia Chiriboga:**

Agreed. Another aspect that sometimes not realized how much it affects motor function is that with decreased mobility and equal consumption of calories there is a tendency for our patients to gain weight. And that actually causes a lot of problems with regards to their mobility. And even though they might have improvement in muscles, they might not be able to perceive it, so it's important to keep that in mind. And to know that the percentile weights are all different with SMA and that you should be in the 10th percentile and that 50th percentile means if you're a type 2 that you may have excess fat that it would be worthwhile trying to limit intake and increase exercise the way Tina was mentioning, because that is very important. And not easy to do and not a lot of resources out there for patients to follow. But when they're able it makes a big difference.

And I've seen improvement during COVID, one young man who lost some weight and was exercising and hadn't been on medication for a while, but he improved just because of what he had done in terms of exercising. So, anything else that either of you would like to ... Okay, so I'm sorry anybody?

**Tina Duong:**

No, no, I was about to say that I think the psychosocial aspect of care in regards to initiation of this paradigm shift in physical activity, or even management of care expectations in regards to start of a disease-modifying treatment cannot be more understated. I think that's something that in general we could help our patients quite a bit to decrease the anxiety related to initiating or maintaining disease-modifying treatment by addressing the psychosocial aspect of it. That I think the adult population is a little bit more unique than the pediatric population that I see that verbalize, at least from the adults that I've seen about care.

**Claudia Chiriboga:**

No, that's a very good point, Tina. And also, when starting treatment, providing realistic expectations. That if you have not been able to move your legs and you are very stiff, you're not going to expect to have a lot of mobility in the legs. But where you do have strength, some strength, that that may improve. And having that discussion about some improvement and stability. And stability is always good because it means that there's a lack of progression that invariably happens with this disease. Let's see about the smart goals. Specific, measurable, attainable, relevant and timely. And I think this is to what you were talking about, Tina, the step-wise care transition and what Vanessa was talking about, the physical, the financial psychosocial needs of youth and young adults. We start that in pediatrics when we start discussing about college, because that's when a lot of these issues come up.

And then to ensure that they connect with an interdisciplinary health care professional to provide the individualized care that is important for adults with SMA and to use and leverage the social services and the community advocacy groups to address the psychosocial needs that you were talking about that our patients do run into. And oftentimes it's starting college. Because they're going from unknown to an unknown. Or for those who are in college the transition to adulthood and independent living and having a job. All of those are very anxiety provoking. To ask a question you can select the ask question tab and we have a few questions. So let me go. Let's say, we have a few. Many patients with SMA struggle with isolation and depression. Any recommendations for management?

**Vanessa Battista:**

I would say, if it's okay to chime in here, I would say-

**Claudia Chiriboga:**

Of course.

**Vanessa Battista:**

... the recommendation would be to make sure that you get appropriate psychiatric or psychologic care for that. There is a distinct difference between anxiety and depression that's sort of inherent with living with chronic illness. And then there is actually anxiety and depression that needs to be diagnosed and treated. And I think it's something that we often feel people know how to prescribe one medication for depression or anxiety. And so we do it among all the other things we do. But we really deserve for people to have a full psychiatric evaluation and to be managed appropriately. Anxiety and depression is just as severe of a, or not even severe, but something that should be taken as seriously as any other part of medical treatment and one's condition. So, I know it is hard to get mental health services and there's often a long wait list, but I would always advocate for getting actual psychiatric care and an evaluation.

**Claudia Chiriboga:**

Absolutely. And we do surveillance for that and we make referrals. My experience is anxiety is more of a problem with our SMA patients than is depression. Though we do have a handful of patients with depression and psychological therapy, as well as psychiatric is important as well. I'm not sure I understand, but maybe you can assess limits of physical therapy. Does that impair patients? Not sure I understand what's being-

**Tina Duong:**

I think it's more, I mean, I don't know. I'm going to interpret it as combination, using physical therapy in combination to disease-modifying treatment. There aren't any studies that say disease-modifying treatment in addition to physical therapy or exercise improves functional status, decrease the progression rate at all. But if we look at kind of a more physiological common-sense approach is that if you utilize your muscles, you're more likely to keep them active and healthy.

And so I think one of the things with chronic SMA is that patients don't know how to activate their muscles. We take it for granted that we remember how to do a bicep curl. To bring food to our mouth or our hands to our head. But if you haven't done that for 30 years, how do your muscles remember to do that? And so when I say a paradigm shift in regards to the physical therapy or rehabilitation approach is that patients almost have to take the onus on themselves to educate their therapy provider. That now there is a paradigm shift in which we don't look at maintenance, we're looking at the possibility of improvement. But I need you to help me in the neuromuscular education realm so my muscles know how to activate in the sequence it needs to be able to perform some of these activities of daily living. Similar to what you would see whenever a rehab therapist is approaching a patient who has had a stroke.

**Claudia Chiriboga:**

Thank you. Let's-

**Tina Duong:**

... those are the things.

**Claudia Chiriboga:**

Let's move to one of the questions because we're almost out of time, so I'll just answer quickly. PCP, different approach to treat comorbidities. There really is none with SMA just to know that there might be dysautonomia that might cause some variability in your blood pressures. And that you need to be mindful if the patient is on risdiplam or medications that are MATE substrates. Because that can interfere with their ability to have the right level. And then the question, how to choose between these two medications? And the last 20 seconds is there really is no head-to-head comparison in terms of efficacy. What we do know is that it's a conversation to be had about side effects, the ability to access, and patient preference. Oftentimes for me it'll be, if there are respiratory issues, sometimes it's a little easier with risdiplam because it has a better distribution.

**Claudia Chiriboga:**

But with that, we are going to have to end our session. And I apologize for not getting to all of the questions. I wish to thank Vanessa Battista and Tina Duong for participating in this lively discussion. And I would recommend that you visit the Virtual Education Hub for free resources and education for health care professionals and patients. And there's the link. And to receive credit, you can click on the “Request Credit” tab, and to process the certificate. And with that, I'm going to thank you for your attention. Thank you, Tina. Thank you, Vanessa. And thank you for your participation.