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Reevaluating Spinal Muscular Atrophy Therapy: Signs, Tools, and Strategies

Announcer:
You're listening to *Neurofrontiers* on ReachMD, and this episode is brought to you by Biogen Inc. Here's your host, Dr. Brian McDonough.

Dr. McDonough:
Welcome to *NeuroFrontiers* on ReachMD. I'm Dr. Brian McDonough, and joining me to share strategies for reassessing treatment response in patients with spinal muscular atrophy, or SMA for short, is Dr. Nancy Kuntz. She's an attending physician in the Division of Neurology, the Medical Director of the Mazza Foundation Neuromuscular Program, and the Director of the Muscular Dystrophy Association Care Center at Ann and Robert H. Lurie Children's Hospital of Chicago. She's also a Professor of Pediatrics and Neurology at Northwestern University Feinberg School of Medicine. Dr. Kuntz, thanks for being here today.

Dr. Kuntz:
Yes, it's my pleasure. Thank you.

Dr. McDonough:
To start us off, Dr. Kuntz, can you give us some background on why ongoing therapy reassessment matters, even among stable SMA patients?

Dr. Kuntz:
The natural history, which has been well outlined in spinal muscular atrophy, documents that there is a slowly progressive loss of motor neurons in untreated or incompletely treated spinal muscular atrophy. And I am part of a crew that is very excited by all of the disease-targeted therapies that have been introduced in the last decade to treat spinal muscular atrophy. However, none of them are a cure, and most of them have been introduced when there's already ongoing disease activity.

There's a little bit of variability between people, even when they have relatively similar ages at onset or the same numbers of backup copies of SMN2 gene. So I think that being able to have both subjective or patient-reported outcomes and objective outcomes relating to motor scale scores, or a measurement of compound muscle action potentials, is very important so that we can determine whether there's any progression that would indicate a potential benefit from more aggressive treatment.

Dr. McDonough:
So then, given that importance, what early signs or functional changes should raise a red flag that we may need to reevaluate a patient's current treatment plan?

Dr. Kuntz:
Well, again, the natural history of spinal muscular atrophy is one of ongoing progression. As we used to say years ago, children with spinal muscular atrophy never learned any new motor tasks after the point of diagnosis. The disease-targeted therapies have changed that, have tended to allow very young children to make motor improvements, and have allowed people with more chronic disease to at least stabilize and not lose any further motor function.

So I think that loss of any previously well-practiced skills or inability to do them as long or reliably as they always have been or have done in recent weeks or months are things that should make us look very carefully at the wellbeing of the person to see if they are, in fact, experiencing disease progression.

Over time, it's very important to recognize within spinal muscular atrophy that it's not one size fits all and that there's quite a bit of variability between individuals. So if an individual has been provided with a treatment, but even despite that treatment they seem to be not doing as well as they have over time—certainly if they lose any skills—but even sometimes when they're just lacking endurance and beginning to not be able to live as full a day or accomplish as much as they had been. That happens to all of us as we age, but I think that it's always worth a look to see whether it is, in fact, something extraneous in terms of their health, or whether it may be spinal muscular atrophy actually progressing.

And this is very important now because we have additional treatments available, so that while there may be some individuals who do very well with a single disease-targeted therapy, I'm firmly convinced that there are other individuals who have more aggressive disease and who need to be treated with multiple types of medication with different mechanisms of action in order to prevent them from having progression of their disease.

Dr. McDonough:
Well, as a follow-up to that, how does our evaluation of treatment response differ between adolescent and adult patients?

Dr. Kuntz:
It really probably depends more on the level of function that the individual has rather than just their age. Because we now have individuals having long survival with spinal muscular atrophy, so we have some adolescent and adult patients who have very severe weakness from spinal muscular atrophy, whereas in the past, we only would see individuals with very mild disease at that age.

So I think that part of it would be to make certain that we're monitoring, targeting, and quantifying the functions that are important to the individual in terms of their independence and their function. As I mentioned, for some people, it may be their use of a joystick or their fine motor manipulation. For others, it's their upper extremity or respiratory function. And then for the most capable or least weak individuals with spinal muscular atrophy, it would be large motor activities like walking, running, distance, stair climbing, and things like that.

Dr. McDonough:
For those just tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Brian McDonough, and I'm speaking with Dr. Nancy Kuntz about monitoring and responding to functional changes in patients with spinal muscular atrophy, or SMA.

So Dr. Kuntz, if we continue focusing on assessment strategies, are there any clinical tools that can help us spot evolving patient needs?

Dr. Kuntz:
Many of the scale scores and timed function tests that have been introduced over time by physical therapists and used in some of the clinical trials can be very helpful. For example, again, objective assessment in a timed function—something like a four-stair climb can be timed. For young children, we can time the time to get up and stand from being supine on the floor—so supine to standing. There's Timed Up and Go test, or TUG, which just involves sitting in a chair, standing up, walking across the room, turning around, and coming back and sitting down, and then either doing that once or repeating it several times to see if there's a deterioration in the amount of time it takes to do that task. So timed function tests are a very important and reasonable way to monitor ongoing capability or strength.

In addition, there are more formal scale scores. For very young children, the CHOP INTEND has been used. Once children get to be sitting and rolling and standing, the Hammersmith Functional Motor Scale—and there's an expanded version that has been used particularly in spinal muscular atrophy. There are upper extremity scale scores, something called the PUL—Performance of the Upper Limb—or RULM, which is an upper limb module that monitors strength and function in the upper extremities, as well as formal pulmonary function tests. All of these have been used very successfully to monitor abilities.

Again, one of the things that's very important with spinal muscular atrophy is to recognize that having absolute stability at these scales is sometimes a real triumph, because by nature, spinal muscular atrophy is a progressive disorder. So maintaining stability is a positive outcome.

Dr. McDonough:
Shifting gears for a moment, what systemic or logistical barriers interfere with timely reassessments or treatment adjustments? And how can we work around them?

Dr. Kuntz:
Well, that the fact that many individuals travel some distances to their care team is something that also interferes with reassessment on a formal basis.

And so this means if we want to carefully monitor progression of disease or wellbeing of individuals with spinal muscular atrophy, if we can start adding in some remote or digital outcome measures, that would be very helpful. Anything we can do to keep people active and in their lives, rather than in the clinic, would be great.

Dr. McDonough:
Before we wrap up, Dr. Kuntz, how can we encourage more open, ongoing conversations with our patients to ensure changes are caught early and addressed effectively?

Dr. Kuntz:
Well, open-ended questions really help a lot, because if you can get your patients comfortable, they'll tell you what's on their mind. And usually I find that what comes out is what they've noticed that's a difference in their daily functioning. So sometimes a problem might even be just a subtle change in mobility, but it's something that is making it more difficult for them to, say, independently toilet because of the physical effort involved, or the fine motor manipulation that's required with snaps and buttons and things like that, or just the self-care that's involved.

And I think that those are the sorts of things that are very important to patients, but many times aren't included on typical patient-reported outcomes, and they're certainly not included in any of the objective measures that we frequently put our patients through to monitor their care over time. But if you give them that opportunity to share with you how things are going and has anything changed, most of them will come out with some very frank and very helpful comments about how they're functioning on an everyday basis.

Dr. McDonough:
With those key strategies in mind, I want to thank my guest, Dr. Nancy Kuntz, for joining me to discuss how we can best reevaluate and adjust treatment for patients with spinal muscular atrophy. Dr. Kuntz, it was great speaking with you today.

Dr. Kuntz:
Thank you very much for having me.

Announcer:
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