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Clinical Advances in Adult Growth Hormone Deficiency: Patient-Centric Approaches to Improve Adherence

Announcer:

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Here is Dr. Kevin Yuen

Dr. Yuen:

What measures can we take to improve clinical outcomes and treatment adherence when managing patients with adult growth hormone deficiency? And how can we improve the therapeutic alliance with our patients to ensure their engagement and ownership of their treatment plan? So those are just a few of the questions that we will be addressing today. This is CME on ReachMD, and I'm Dr. Kevin Yuen.

Dr. Hoffman:

And I'm Dr. Andrew Hoffman.

Dr. Yuen:

Welcome, Andrew. As you know, the diagnosis of adult growth hormone deficiency can be quite complicated at the primary care level in identifying patients who may be struggling with this disorder and even for the specialists. So what are the telltale signs to look for? And if you suspect adult growth hormone deficiency, what do you do in this situation?

Dr. Hoffman:

Well, when thinking about adult growth hormone deficiency, the patient population at risk are those who had had childhood-onset growth hormone deficiency and individuals who have pituitary or brain tumors. The most common patients that we see are patients with pituitary adenomas and patients who had a history of severe traumatic brain injury. The signs and symptoms of adult growth hormone deficiency, unfortunately, are fairly diffuse and nonspecific. Patients complain of decreased energy, decreased muscle mass and strength, decreased ability to do exercise and their normal workload, and often they complain of social isolation and a poor quality of life. If you have a patient with pituitary disease who has these symptoms, it's important to evaluate them for hypopituitarism. This involves getting standard pituitary function tests like thyroid function tests, adrenal function tests, and an assessment of sex steroid production. In addition, as a screening test, I usually order a serum insulin-like growth factor 1 (IGF-1) level. The IGF-1 level is a reflection of growth hormone secretion, and if the IGF-1 level is low or in the low part of the normal range, I then think that they are good candidates for evaluation for adult growth hormone deficiency.

Dr. Yuen:

Excellent points, Dr. Hoffman. I think the next thing we need to do is also to confirm the diagnosis, and this is done by doing a growth hormone stimulation test. And there are several options or several different types of tests that one can consider: the insulin tolerance test, the glucagon test, and more recently, the approved oral macimorelin test. So they all have their own individual pros and cons in

terms of conducting these tests, and certain centers are only able to do these tests because of these limitations. But certainly, they need to be performed, and once the test is done and once the diagnosis is confirmed, then there's a reason to consider treatment for these patients.

So, Andrew, what can you tell us about the many other barriers to care that we find in managing adult growth hormone deficiency?

Dr. Hoffman:

Well, Kevin, once we make the diagnosis of growth hormone deficiency, we have to have a conversation with the patient to see if the patient is willing to take daily injections of growth hormone. While these aren't painful, it does represent a major change in a lifestyle, and this is something that many patients are simply not willing to do. Once they've agreed to do it, the next barrier has to do with the cost of the therapy. While most insurance plans will cover the cost, the copays can be high, and it takes quite a while for the insurance companies to provide prior authorization so that the therapy can begin. Every year, the clinician may have to reapply for prior authorization to keep the patient on therapy. And these are some of the things that make diagnosing and treating growth hormone deficiency somewhat difficult. Patients may also not really recognize that they have the symptoms of a growth hormone deficiency. It may be somewhat subtle and in fact, I have a number of patients who have told me after being on growth hormone for many months, that they only recognized how poorly they were feeling once they got the therapy and were really improved greatly. Another barrier is that we tell patients that this is a therapy and not a cure and that they will have to take growth hormone for the rest of their lives.

Kevin, let me ask you about some new aspects of the treatment of adult growth hormone deficiency. We know that our current therapies are very efficacious, but they certainly have some significant limitations. What do you see as the major differences between our current treatments and some of the emerging therapies like long-acting growth hormone preparations?

Dr. Yuen:

Well, again, like I alluded to earlier, Andy, the growth hormone treatment that currently is available is a daily injection, and patients do often find it somewhat cumbersome to do that, especially if they lead a busy life. Or sometimes, if they are having many medications that they have to remember to take in a timely manner, and so injecting another injection where they, perhaps, in the short term may not actually see the benefits of treatment, can be sometimes difficult for them to appreciate. So in the recent times, obviously, there has been a lot of research to address that unmet need, which is to see if we can help improve the adherence of daily injections, hence the many studies in the last five to ten years looking at long-acting growth hormone preparations. And that has been done by several companies. Several different preparations have been looked at, and the results—and some of them have been extremely encouraging. And so we look forward to seeing that. It would be hopefully becoming available in the near future, although at this moment in time, it's still not available yet. But if that—and when that becomes available, I think it's going to help address that very important issue, which is the adherence part of it, which I think many of our patients face when they're giving these injections on a daily basis every day.

Dr. Yuen:

So for those who're just turning in, you're listening to CME on ReachMD, and I'm Dr. Kevin Yuen, and I'm joined by my colleague, Dr. Andrew Hoffman. We are discussing limitations of current growth hormone replacement therapy and the role of emerging long-acting growth hormone formulations.

Dr. Hoffman:

So, Kevin, I'd like to actually focus even more specifically on some of these new long-acting formulations. Can you tell us what you expect to see in the very near future and how you think they'll play a role in our armamentarium against growth hormone deficiency?

Dr. Yuen:

Sure. There have been several studies looking at seeing how the action of growth hormone can be prolonged in order to improve the—or prolong the action of growth hormone at the level of the receptor, and certainly, there's a couple of technologies that are now being studied. There's a pro-drug formulation call—and one of them is called the TransCon Growth Hormone manufactured by Ascendis Pharma. And then there's also another product by Novo Nordisk called somapacitan, which, essentially, where the growth hormone molecule is attached to albumin in the bloodstream. Now, these two compounds have been presented in conferences—certainly the data has been presented in the conference, in recent conferences—and some of the data has also been published. And in the summary, I think the results have been extremely reassuring and optimistic in that there has been no reduction in terms of efficacy compared to daily growth hormone, both in terms of looking at children and also looking at adults.

So, I think it's reassuring that these compounds are doing what they're supposed to do, but there's also some caveats associated with these long-acting preparations. And the reason I say that is because these long-acting preparations may not have the same molecular structure because they are made up of different molecules in order to prolong their action. So different long-acting preparations may require different regimens in terms of monitoring the efficacy of these compounds. And there's also the possibility that the molecular sizes of these compounds may not be the same, so there's also an issue of tissue penetrance in different types of tissues in—be it in

the bone or in the adipose tissue. So that might somewhat explain some of the differences in the data that we've seen concerning other long-acting preparations whereby some of the endpoints were not necessarily met. But so far, I think these two compounds seem to be pretty reassuring, and I'm pretty optimistic that they will hopefully in—one day when they are approved—fill the unmet need of helping patients address the need—the issue of adherence and compliance to daily growth hormone injections.

Dr. Hoffman:

Well, I've been equally excited about the possibility of having a long-acting growth hormone preparation, and I think that the published studies have conclusively shown that in the short run, that these growth hormone products are equivalent in efficacy to that of the daily growth hormone. However, I think we have to recognize that these are short-term trials, and it'll be important for us to see whether these drugs remain as efficacious over the long run. Moreover, since these growth hormone molecules have been modified to some extent, we have to be careful to see whether there are going to be any new side effects that appear from chronic use of the drugs. In particular, I'm concerned that having high growth hormone levels for a prolonged period of time might lead to some acromegalic changes after years of therapy. Because of this, I think it's very important for the drug manufacturers to do careful follow-up studies once the drugs have been approved. I think that these drugs will really take over the market because they are much more convenient, and I think that many patients who are so reticent to take daily shots would be much more willing to take a weekly injection.

Dr. Yuen:

Very excellent points. I agree. I have also had the same response with my patients, that there is a light at the end of the tunnel, especially patients who are on many other injections that they take, for example, if they are on insulin injections or they're on testosterone injections. So to give them the option of a once-a-week option of injections, certainly, it does help them improve their enthusiasm, I should say, in terms of going forward with continuing with growth hormone preparation—the growth hormone therapy.

So, Andrew, we frequently discuss ways to enhance shared decision-making in clinical practice. So where are the opportunities, do you think, for shared decision-making in adult growth hormone deficiency? And how have you made it work in your practice with your patients?

Dr. Hoffman:

Well, I think it's my job as the physician to explain what adult growth hormone deficiency is and to try to work with the patient to decide whether they actually have any of the signs of growth hormone deficiency. If they have decided that they don't want to do the daily shot, I tell them that I'm going to bring up the question again in the future and that they should consider it. And when we decide to start growth hormone, I have to tell them several things—first of all, that they should commit to taking the drug for at least six months because it will take a while before the drug's full effect will be noticeable, and that I commit to monitoring their therapy carefully, and that my clinic and I commit to helping them with the insurance companies to get prior authorization. And if, in fact, the cost is prohibitive for them, that we will also try to work with them to find ways that the companies have for mitigating the cost. I think it's important not to be judgmental with the patients on this and to discuss and find out what their fears and concerns are about taking growth hormone therapy.

Dr. Yuen:

Excellent points, Andrew. I agree with you. I have also had that opportunity to talk to my patients. It's important to spend time educating them, and sometimes their fears need to be allayed to the fact that it is growth hormone, and it has a good track record so far, at least in terms of safety. And so some of these patients who go on it are somewhat concerned. So I talk to them and also give them the data on safety, both in terms of recurrence of tumors, new cancers, new tumors that may occur in the brain. And all these have been studied in large epidemiological and large registry-based studies, and they've all been reported to show that growth hormone has been safe in this regard. So I think the safety aspect is also very helpful when we are discussing this issue of growth hormone—long-term growth hormone replacement with these patients.

So, well, this has been certainly a very valuable conversation that I've taken away, and before we wrap up, Andrew, can you share with our audience the one take-home message that you want them to remember from our discussion?

Dr. Hoffman:

I think it's very important for practitioners to recognize that even though it may be difficult to diagnose and to prescribe growth hormone, and while the signs and symptoms of growth hormone deficiency may be subtle with even the patients not recognizing their need for growth hormone, the drug is really very efficacious. Many patients find that their quality of life is greatly enhanced with growth hormone therapy. It's a safe therapy, and there are many endocrinologists who are happy to help with prescribing for those practitioners who don't feel comfortable in making the diagnosis themselves.

Dr. Yuen:

That's great. And from my vantage point, I think one of the biggest takeaways from today is that growth hormone is safe. It exerts beneficial effects in various areas, such as body composition, such as quality of life, such as metabolic abnormalities. So all these

factors are very important, especially as patients get older, because these are issues that are certainly going to be very prominent in their life. And certainly, they want to know that their daily injections—at least for now it's still daily injections that we have—is worth their efforts and their fruits of their labor.

So unfortunately, that's all the time we have for today. And so I want to thank our audience for your participation and also my sincere thanks to you, Dr. Hoffman, for kindly joining me today and for sharing all your valuable insights and your wisdom on this topic. It was great speaking with you today.

Dr. Hoffman:

Well, thank you, Kevin. I enjoyed speaking with you and with our audience today.

Announcer:

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