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Neuromodulator Dosing for Duration

Announcer:
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Here’s Dr. Joel Cohen

Dr. Cohen:
Despite sharing a similar mechanism of action and efficacy profiles in some cases, there are 4 different currently available neuromodulators on the market. I’m Joel Cohen from Denver, Colorado. I’m a board-certified, fellowship-trained dermatologist, and I’m excited to be with Dr. Carolyn Jacob from Chicago, who’s also a board-certified, fellowship-trained aesthetic dermatologist. Carrie, thank you very much for joining us.

So, let’s dive right in. Dr. Jacob, can you give us an overview of the currently available botulinum toxin products that we have available in our practices?

Dr. Jacob:
Thanks for having me, Joel. Yes, so it’s a really exciting time to be a dermatologist. Those of us who’ve been practicing for a while remember the off-label-use days when all we had was onabotulinumtoxin, but now we have abo, we have ona, we have inco, and we have prabotulinumtoxin. And hopefully coming up later this year, we’ll talk about in a minute, daxibotulinumtoxin. So there’s 4 on the market in the United States currently, and we use them all in our office because I kind of look at it as people liking Coke versus Pepsi versus any of the other colas. People kind of have their favorites from their experiences. How about you, Joel?

Dr. Cohen:
So we’ve actually done the clinical trials, as you have, on all 4 products, and sometimes patients ask for a specific product, perhaps if they were in the clinical trial or they know somebody who’s had a good experience with the product in the past, such as a friend or a sister. But there are main products that we carry in the office that seem to be, certainly, a bit more popular. People who have that name recognition with Botox, and Dysport is really popular in our practice, as well, and represents about half of all patients who get treated with neuromodulators in our practice.

Dr. Jacob:
I agree, and there are some subtle differences between these 4 products that we have available. Even though they all have the same 150 kilodalton molecule, they have different epitopes on them, so people seem to have a little bit different experiences with them. One of the things that I find interesting, and when I’m explaining it to a new patient who’s coming in to see us, is the fact that we do have those clinical trials showing that abobotulinumtoxin sets in in about 1 to 5 days, and its duration in those clinical trials was also slightly longer than those of onabotulinumtoxin. I also extract that to we have some off-label uses that we use these toxins for, one of which is the treatment of hyperhidrosis. And in those studies with abobotulinumtoxin, the duration was about 30 days longer than that of onabotulinumtoxin. So I usually have those conversations with patients if they are a brand-new patient trying to decide, again, what

product they want to choose.

But we do find that all of them are effective. I've used all of them on myself because, of course, when we get something new, we want to see for ourselves how it works. And I find that patients are very satisfied with their treatments. There's a few differences in terms of the FDA approvals, of course, of these different neuromodulators, as I like to call them. Whereas onabotulinumtoxin is approved for the lateral canthal lines as well as the glabella, the other products are currently approved for the treatment of the glabella.

Dr. Cohen:
So with onabotulinumtoxin specifically having upper face indications – glabella, crow's-feet, as well as forehead – you know, that's something where I think people are aware that you can use these neuromodulators in many different areas. And with ona actually having those 3 indications, do you think that that's a barrier for people who may be interested in some of the other neuromodulators and think about FDA indications?

Dr. Jacob:
So the nice thing is, as dermatologists, we are allowed to use our clinical judgments to use different products off label, as long as we know that they're safe and effective. And because you and I have been doing this for so long with so many of the products, we do know that all of them are safe and effective for the on-label areas, as well as other off-label areas. Because I know you are a master at this and I'm sure you, like we do, treat the platysma muscles and the depressor anguli oris and the masseters for narrowing of the face. So there's a lot of areas that we constantly are using these neuromodulators for in a safe way for our patients. So I think that we, as practitioners, have the confidence in using all of the neuromodulators in different areas.

Dr. Cohen:
So for people who may be interested in transitioning a patient from one neuromodulator to another, can you talk to us a little bit about that conversation and how you position things?

Dr. Jacob:
Yeah, and it's interesting because, again, after doing this for over 20 years, I do find that some people feel suddenly the product that they were using doesn't last as long, and there's a lot of myths out there that say, oh, if you use it longer, it's supposed to last longer, or your muscles will get more weak and your duration will be extended. And a lot of times, people just want a change, and so they're interested in seeing if something else will be better. And a lot of times, we are switching between either abo to ona or ona to abo because those are the ones we most commonly use in the office, too. However, I do have some people where we've moved on to a third or a fourth just to give it a try. And again, there's these slight differences in the patient's responses to the neuromodulators that I think are unique and individual. And I don't think that we've yet ferreted out exactly why some people do better with one product versus another. And so that might be some very interesting area of research for the future, as well.

Dr. Cohen:
So in terms of that, there is really the reality of combination therapy. We all use many different products in our practices in terms of giving patients a great overall aesthetic effect, and everybody wants to focus on, really, a natural look. And I agree with you, the forehead is an area that, even though the FDA study that I participated in for onabotulinumtoxin was 20 units specifically, it's very common for me to use 4 or 5 units in these micro aliquot dosing, where I oftentimes reconstitute it higher to really pepper the forehead and sort of have these little areas of softening the musculature.

You know, I think that incorporating resurfacing into practice is important, as well, whether it's non-ablative or ablative, and I think that we can help with that pre-juvenation, as well, especially with non-ablative. And then when people do have etched lines, using a combination of ablative fractional resurfacing and full-field resurfacing can really give people a nice improvement.

So can you talk to us about your technique for combination therapy and optimizing effect using a neuromodulator plus filler and using a neuromodulator plus laser resurfacing?

Dr. Jacob:
Sure. So we really like to look at the patient as a whole and decide what lines are there because of muscle movement, obviously, and then what lines might be etched in or there because of volume loss. And so a lot of times, we are doing both, using a neuromodulator and a filler on the same day. And I have absolutely no problem with doing both in similar areas. The one thing that we often try to avoid is when we're doing a laser resurfacing of some type, I like to get that neuromodulator in 2 weeks prior to the actual laser treatment. That way, the muscles are relaxed and they're not going to crease over the newly treated skin because we really want that collagen to grow and not have an opportunity to re-crease, especially if you're talking about the forehead. I also do love your description of peppering across the forehead. I call it sprinkling, but I'll do the exact same thing, where I will take a very small amount of neuromodulator and put little, tiny bits across the forehead to soften the look without preventing the movement.

And one of the other interesting things, when we were talking back about pre-juvenation, is that we've got these younger patients who are looking at themselves in Zoom, and they want to make sure that they don't get these lines or they're just starting to see lines. And an interesting study that we both just participated in showed that patients who were given 50 units of abobotulinumtoxin to the glabella had really great satisfaction, like 95% or more satisfaction, in having that treatment done just every 6 months. So it'll be really interesting to see kind of what evolves in the future here, knowing that daxibotulinumtoxin, which is a little bit different neuromodulator because it has a carrier molecule attached to it to potentiate its effect, and its clinical trials were showing efficacy up to 6 months, whereas the other neuromodulator clinical trials were showing about 3 to 4 months. So it'll be interesting to see how many of our patients we transition to something that we know lasts 6 months because of potentiating carrier molecule as opposed to some of these pre-juvenation people that are already satisfied with treatments just every 6 months. It's really interesting.

Dr. Cohen:
For those just tuning in, you're listening to CME on ReachMD. I'm talking to Dr. Carolyn Jacob from Chicago. I'm Joel Cohen from Denver, Colorado, and we're really overviewing botulinum toxin agents and talking about dosing and duration.

So let's get more into dosing for duration. And, Carrie, can you talk about some of the recent abstracts looking at higher-dose neuromodulators?

Dr. Jacob:
Sure. So several trials are underway showing differing responses to higher doses than what's on label for the different neuromodulators that we have. So for instance, onabotulinum looked at 40 and 60 and 80 units in patients to the glabella only. And they had about 225 female patients in their study, and they were just looking at a 1-grade improvement. And it was interesting, because even when they doubled, tripled, or quadrupled their dosing, it didn't seem to increase it more than about 30 days. So in looking at the numbers, it was kind of like your regular dose was to last about 5 months, but double the dose was 6, triple the dose was 6, and quadruple the dose was also 6 months. So I found that that was very interesting.

Then incobotulinumtoxin, there was also a study done with only 151 subjects looking at different doses between 20 units, 50 units, or 75 units. And again, a 1-grade improvement in these patients. And they saw that in their original 20-unit dosing, which is on label, their 1-grade improvement went out to 6 months, but at 50 units, it went out a little further. But at 75 units – you're really jacking it up here, it's like 3 3/4 times the amount of product – it was only 7 1/2 months for that 1-grade improvement. So again, pushing it further doesn't seem to really give you a linear duplication or triplication of the lastingness of a 1-grade improvement.

And then finally, abobotulinumtoxin did a study with a much larger group, 399 subjects that were randomized, and they looked at 1-grade improvements. And what was very interesting – the on-label for abobotulinum, of course, is 50 units to the glabella. And they found that that lasted about 32 weeks or 8 months. So again, a lot of times we're telling patients that it's going to last 3 to 4 months. But that's the 2-grade improvement that allowed them to get their FDA approval. When you look at a 1-grade improvement, it goes out even further. And then when they pushed it out to 75 units or 100 or 125 units, it went up to about 9.15 months. So again, you're pushing it a little bit, but what I found astounding was when you just looked at the regular dosing for the 1-grade improvement, that it almost looks like there's no point in trying to double-dose anything else because the 50 units of abobotulinumtoxin lasted longer, had a 1-grade improvement longer than the other 2 products anyway.

So what were your thoughts?

Dr. Cohen:
So, Carrie, let's unpack a little bit of this. So first of all, the onabotulinumtoxin Botox study that was actually discussed was at the ASDS [American Society for Dermatologic Surgery] was an abstract. So if we look at that – Sue Ellen Cox's data from 20 versus 40, 60, and 80, the 40, 60, and 80 really extended the duration from about 19.7 weeks at 20 units to actually 24 weeks with the 40, 60, and 80. So I'm just wondering how you would phrase this to a patient. "Hey, to get 4 more weeks' duration, it's going to be possibly twice the expense." How do you think that's going to work in clinical practice?

Dr. Jacob:
Yeah, that's exactly my thought about it. And again, in seeing these numbers, one might think if someone's complaining, "I don't think this lasts long enough for me," that one should consider switching them from ona to abo that seems to have a better 1-grade improvement that lasts longer. So those are more of the conversations that I have. I don't talk about weeks or months because nobody wants to look at their calendar and follow it that closely. However, just given the clinical data that I keep seeing again and again, if people are thinking that something doesn't last long enough, then I think they actually need to switch products.

Dr. Cohen:
And I agree with you. And at least in my practice, patients don't like to hit rock bottom, so they don't want to let things completely wear

off. So they're not necessarily interested in the longest stretch of time, but they really want to know how long something is going to look good.

Carrie, I want to thank you for joining us for CME on ReachMD. It's been a pleasure to talk to you today, and I look forward to talking to you again.

Dr. Jacob:
Thanks so much, Joel.

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