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Battling Depression with Botox? A Look at the Potential Mental Health Benefits

Dr. Greenberg:

Botox is a well-known rejuvenation treatment that can help our patients look and feel younger, but could the effect of this treatment go beneath the surface and help our patients who are struggling with depression?

Welcome to *DermConsult* on ReachMD. I'm Dr. Michael Greenberg, and joining me today to discuss his recent study focusing on the potential mental health benefits of Botox is Dr. Ruben Abagyan, a Professor of Pharmacy at the University of California-San Diego.

Ruben, thank you for being here today.

Professor Abagyan:

Yes, thank you for inviting me for this interview. I'm excited to talk to your listeners.

Dr. Greenberg:

Well, our listeners are excited to hear this, so let's just jump right into this. Tell us first about your educational background and how you got involved with the idea of Botox relieving depression.

Professor Abagyan:

I'm a physicist and mathematician, and I migrated to biophysics and so on, and then basically I like the theoretical ideas, calculations, math, and then I was spending a lot of time in drug discovery, but when I ended up in the School of Pharmacy, I started looking into repurposing drugs for different indications, and the FDA data gave me this opportunity because it's a maximum amount of reports to the FDA, about 14 million right now, and then you can actually find all kinds of unexpected connections. And then secondly, Botox just showed up as one of the signals, but the severe depression I was attracted to because it's really a deadly condition, and there is no treatment. There is no short-term immediate relief against depression.

Dr. Greenberg:

Okay. Do you have any colleagues in this study with you?

Professor Abagyan:

Oh, sure. The first author is Tigran Makunts, who used to be a student at the School of Pharmacy and Pharmaceutical Sciences, so now he's at the FDA, and the second author, Marc Axel Wollmer, is a prominent clinician from Hamburg, Germany who helped us to basically keep it real because he has vast experience in botulinum toxin treatments.

Dr. Greenberg:

Okay. So I always envision Newton sitting there under a tree, and an apple falls, hits him on the head, and he goes, "Oh, gravity; let's study that." So, in this case, what was the apple that fell from the tree? Who kind of spoke up one day and said, "Hey, look at this; Botox is keeping people happy"?

Professor Abagyan:

I'm, of course, not Newton by any stretch of imagination, but I think the key observation here was that we can look at some bad data about adverse effects of drugs, but then you can look at that from a positive standpoint and observe the reduction of bad side effects rather than the appearance of bad side effects, and once that idea came to mind, we started systematically looking for beneficial effects of drugs on unexpected aspects of your health, and botulinum toxin just jumped just right out of that.

Dr. Greenberg:

Having said all of your background here and knowing what you're doing here, can you give us an overview of the premise that Botox lowers depression?

Professor Abagyan:

Okay, so there are two things. There's one, the observations, whether it really lowers depression, and second is explanation, why it lowers depression or why it may lower depression. In terms of the observations, in our study we basically looked at every drug or treatment for which we observe a much lower depression background level, and in this study we found basically four different things. One was ketamine, and it was published a few years ago, and then a few years after that Spravato was approved for depression treatment, and that's a ketamine. So the second one was botulinum toxin, and it was pretty clear there were two other ones. After we published the paper, which was primarily focused on ketamine, we decided to look further into botulinum treatment because it was not clear to us if it just needs to be only one location, only one muscle connected with that magic nerve which is linked to depression, or it basically has a particular dependence on the site of administration. We were curious to look into that particular aspect, and that's the second basic tier. The first tier was just observing the overall botulinum toxin treatment leads to a significant drop in complaints about severe depression, and then the second was to look into details, because botulinum toxin is used for many different indications, and we were curious if there's a preference.

Dr. Greenberg:

You haven't found one nerve, as you mentioned there, correct?

Professor Abagyan:

Indeed, we found that the effect goes beyond one nerve. We made a positive observation that botulinum toxin is basically a toxin—that's why it's called a toxin—and it kills the connection between a nerve and a muscle, and in most cases its current use is to kill that connection and make a muscle flaccid, so if you have some local muscle which is overactive—and overactive muscle in different parts of the body causes very different clinical effects—so then you can actually treat that with botulinum toxin. We noticed that there is a connection between the state of some of your muscles and your happiness, and so the theory is that there is basically, let's call it, a mind-body connection. In other words, your mind outsources the memory about its depressive state to some muscles, and then, when the mind is distracted and does something else and then comes back and asks itself "Am I happy or unhappy?" it looks into that muscle, and the muscle says, "Well, you're unhappy, continue to feel so," and that creates this feedback loop.

Now, what we found is that connection is not located to just one frown wrinkle in the face, but it can be even a muscle in your limb, and broadly it can be perceived as the distributed mind-body memory and that may be one of the explanations why what we observed was that the antidepressant effect doesn't really depend strongly on the site of the injection.

Dr. Greenberg:

For those just tuning in, you're listening to *DermConsult* on ReachMD. I'm Dr. Michael Greenberg, and today I'm speaking with Professor Ruben Abagyan about the potential benefits of Botox for patients with depression.

So, Ruben, if I play devil's advocate for a moment here, all the conditions that are mentioned in your publication are frustrating and sometimes painful by themselves, so wouldn't relief from them alone be enough to lower depression?

Professor Abagyan:

Right, so that's an excellent question, and there is a very clear answer to that. When we do our analysis, we compare the antidepressant effect of botulinum toxin with another treatment, which leads to the same therapeutic effect or similar to a comparable therapeutic effect. For example, if you have migraine prophylaxis, then you can look at other therapeutic treatments, and we compare and we calculate the ratio, like the effect of botulinum treatment for migraine versus another, and so we calculate these so-called odds ratios between them. For spasticity and spasm, there are other treatments. Therefore, we compared two treatments, one of them being botulinum toxin, another is one of the prevalent treatment with other means, and then we see botulinum treatment improves that. In other words, in both cases your wrinkle is gone or your migraine is gone or your spasm is gone, but then it's only when you treat with botulinum toxin when you observe the antidepressant effect. It's a relative elimination of depression.

Dr. Greenberg:

So, how long has this research been available to physicians?

Professor Abagyan: Generally, it was known for a number of years as a hypothesis. It was not clear which particular type of botulinum toxin treatment. There are many variables here. One is what toxin do you inject, because there is botulinum toxin A, B, E and other ones. The second is the dose and where you treat. For hyperhidrosis, for example, which is sweating, you inject it in the armpit, or for facial wrinkles it's the face, so they could be different places.

Dr. Greenberg:

Are there any physicians who have jumped on the bandwagon that you know that are treating patients for depression with Botox?

Professor Abagyan:

Definitely our collaborator on this paper, Marc Axel Wollmer, liked to do that, and he reports about some clinical observations like that, and I am pretty sure that many clinicians do that in some form. And I think it's difficult because there is no completed clinical trial to have it supported only for depression, because you need to make a choice of where you treat and how you treat, and then you need to prove it in an appropriate clinical trial, which hasn't been completed yet, so therefore, individual clinicians definitely may do that, but it's not widespread.

Dr. Greenberg:

Oh, excellent. That could be a great future use for this really safe medication. Finally, Ruben, what's the next phase of research in this theory? And where do you see this going down the road?

Professor Abagyan:

Well, I think the next step is translation into clinical practice and approval. And through that process I think the optimal site of injection and the optimal dose and the effect and safety can be quantified and justified. I think these are the next steps. Our study simply opens up those clinical trials to a broader range of injection sites and doses.

Dr. Greenberg:

Thank you. I can just see the ads now from dermatology offices. "Look good and feel good at the same time."

Professor Abagyan:

Absolutely, yeah, you got it.

Dr. Greenberg:

Well, that's all the time we have for today, but I want to thank Professor Ruben Abagyan for joining me to discuss this recent study on some of the potential unexpected benefits of Botox. Ruben, it was great speaking with you today.

Professor Abagyan:

Thank you, Michael, same here. I enjoyed our conversation.

Dr. Greenberg:

And please let's connect down the road as more of this research becomes available.

Professor Abagyan:

Will do.

Dr. Greenberg:

All right. For ReachMD, I'm Dr. Michael Greenberg. To access this episode and others from *DermConsult*, visit ReachMD.com/dermconsult where you can Be Part of the Knowledge.

Thank you for listening.