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From Prevalence to Practice: Practical Screening and Workup for Hypercortisolism in Resistant Hypertension

Announcer:
Welcome to CME on ReachMD. This activity is the sixth in “The Cortisol Reports.” This is episode 6, titled “From Prevalence to Practice: Practical Screening and Workup for Hypercortisolism in Resistant Hypertension.” This episode is jointly provided by Cornerstone Medical Education and the American Academy of CME and is supported by an educational grant from Corcept Therapeutics.

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Dr. Plutzky:
Hi everyone. We're here to discuss what's been a very exciting and rapidly evolving area of medicine, namely hypercortisolism. And that interest is really being driven by some new data and insight into hypercortisolism and the implications of hypercortisolism. It's really shifted some of our prior perspectives on how common is it and is bringing clinicians around to revisiting how to identify it, understand what it means to have hypercortisolism, the impact it can have on health, and that raises lots of questions for all sorts of team members providing care for patients about screening, identification, and subsequent interventions to try and improve outcomes.

This is CME on ReachMD. I'm Dr. Jorge Plutzky. I direct preventive cardiology at the Brigham and Women's Hospital, part of Mass General Brigham, and I'm on the faculty of Harvard Medical School, and I'm pleased to be joined today by my colleague, Dr. Brad Eilerman. And Brad, I'll let you introduce yourself and what you spend your time doing.

Dr. Eilerman:
Hi. I'm an endocrinologist. I practice for a large multispecialty group in the northern part of Kentucky. I am also adjunct faculty at the University of Kentucky.

Dr. Plutzky:
Great. And so the new data around hypercortisolism has really been eye-opening to me as a cardiologist, not thinking and dealing with that quite as much before. Can you talk a little bit about, where that data is taking us and these new insights into hypercortisolism?

Dr. Eilerman:
Yeah, it's been very interesting over the last few years. This has been something that a lot of us have been suspecting has been a bigger problem than we had realized in the past. If you look at previous estimates of hypercortisolism, they were not particularly high, although still higher than a lot of people would have thought in the past. Looking at people with fragility fractures, rates were estimated somewhere between 1.9 and 17.6%. People with difficult-to-control hypertension, up to 8%; diabetes 3.4%; obesity a little less than a percent. So happening but not necessarily happening at the level that we felt that we should be screening frequently.

And we know that if we look at people with high levels of cortisol, it's more than just one thing that's going on. And part of this has been driven by the observation that when we see patients that are having poor control despite throwing out all of the very good options that we have, that there's a percentage of patients that exist that are overproducing cortisol and will not get better until we address the cortisol directly.

In the context of the CATALYST trial, patients with difficult-to-control diabetes were given a 1-mg overnight dexamethasone suppression test. We found that patients with difficult-to-control diabetes had hypercortisolism defined by the overnight dexamethasone suppression test at 23.8%—massively higher than what we had previously estimated. And what we found that was even more interesting is that patients that had the overlap with difficult-to-control type 2 diabetes and difficult-to-control blood pressure in terms of taking greater than three blood-pressure medicines, the rate of hypercortisolism was 36.6%.

So this was an issue that we thought absolutely needed to be explored further, and this is where I'd really like to know where cardiology fits in.

Dr. Plutzky:
Yeah. Well, I think, this is really sort of unmasking something that we weren't familiar with. And within the world of cardiology, obviously we deal with these kinds of issues whether we recognize it or not. And so I think the importance of this is sort of the uncovering of a major driver of cardiovascular issues that had previously not been appreciated.

If we look at the data that you've set up so nicely the subsequent studies have really highlighted the extent to which hypercortisolism can be a player in the kinds of cardiovascular issues we're often dealing with. Of course, this is informing the study known as MOMENTUM, which has been looking at patients with resistant hypertension. And the MOMENTUM trial was really an assessment of the prevalence of endogenous hypercortisolism in patients with resistant hypertension. These are, of course, quite standard definitions of resistant hypertension as used by the AHA and other groups.

And so in MOMENTUM, about 1,000 patients with resistant hypertension were studied and analyzed across several visits to whether or not there was or was not the presence of hypercortisolism, and ultimately coming to a conclusion about what the prevalence of that was.

And that's really what struck me, Brad, about this data is that if you think about resistant hypertension, of course we all encounter that all the time clinically almost however we practice, whether it's in internal medicine or cardiology, endocrinology. When you look at the data that came out of MOMENTUM and has now been presented and is being disseminated, when you look at just assembling people with these definitions of resistant hypertension and ask if I study patients with resistant hypertension, how often will I find hypercortisolism? I mean, the results were pretty astounding using a post-dexamethasone suppression test, that the incidence was 27.3% out of that cohort of people not identified for other reasons than that resistant hypertension.

And so for me to think about all the patients in whom we have on multiple drugs for resistant hypertension, that lurking underneath the surface is this 27% incidence of hypercortisolism and that that's not being addressed, that really highlights the fact that this is an important and common issue and that there's, terrific opportunities to maybe intervene and do something about that. Some people had thought, well, maybe there's some other patterns to play at here. The 27% is really astounding, but no, the people with hypercortisolism really didn't look very different than the patients who didn't have it in those MOMENTUM data.

What I find quite compelling within the world of cardiology and as I talk to internists about this and nurse practitioners, other folks involved with internal medicine practices, because of course we're utilizing and relying on these other individuals much more in delivering healthcare, that the prevalence of cardiovascular disease among those people with hypercortisolism is really impressive. So among those 27% who had hypercortisolism, 32% of them had atrial fibrillation, the kind of thing we deal with all the time in cardiology. It's like looking in your yard and seeing weeds. It's like it's everywhere. And to think that these people have basically a 1 in 3 chance of having atrial fibrillation if they have hypercortisolism in the setting of resistant hypertension is very impressive—33.6% of them had coronary artery disease, and 33.6% of them had heart failure.

So this is really the classic kinds of issues that we're dealing with in cardiology all the time. It's just identifying hypercortisolism, resistant hypertension, as being a driver of that.

And we've had also a lot of increasing interest from the American Heart Association and others about the extent to which heart disease is connected to kidney disease and this focus on the CKM syndrome of how cardiovascular disease, kidney disease, metabolic issues all intersect. And there the data has also been quite impressive. When you look at hypercortisolism among people with renal dysfunction, they have worse kidney disease, they have higher levels of urine albumin-creatinine ratios, which is part of that new CKM focus, and they also have evidence for having a greater risk of progressing in their kidney disease if in fact they also have this positive post-DST suppression test.

So I think it's been incredibly important data. Of course, MOMENTUM is just is landmark in its nature, but we note the fact that this was based in the United States. We've had other studies that are a little bit smaller elsewhere in the world roughly similar kinds of incidence and results were study at 26.5%. There was substantial representation of minorities here. There were fewer Asian patients. It wasn't a heart-failure study, MOMENTUM, so we don't have as precise definitions about that. And of course, we'll need additional data to

understand and see whether this is supported elsewhere. This was not a study looking at causation; this is really just a study looking at incidence and prevalence. But I do think from a clinician's perspective that it really does make you realize that you need to think about hypercortisolism even in simple scenarios of like resistant hypertension.

So I think this data is very impactful, it has really drawn a lot of interest within cardiology and other circles. I'm interested, Brad, in how you see these findings out of CATALYST and MOMENTUM impacting practice, whether it's in internal medicine, primary care, family practice, or even within endocrinology.

Dr. Eilerman:
I think it's really important to realize that everyone has a role in identifying something that has such a broad impact with regard to health. I think the thing that really hits home is that this is not a singular process causing a singular condition; this is a process that's impacting multiple systems in the body. We mentioned the metabolic consequences, the cardiovascular consequences. Of course, elevated cortisol goes well beyond that, and so identifying the root cause where we can, gives an opportunity to help a patient on a number of levels.

I think in terms of what we need to be thinking about as an entire healthcare team are the kind of patients that are going to be at higher risk. And that's where looking for the exceptions to the rule, the people that are requiring multiple medications and are still not having success, be it with diabetes with regard to the CATALYST data, if we're talking about hypertension with regard to the MOMENTUM data, and understanding that the Venn diagram where those two particular groups intersect are where the results are particularly enriched.

So, I know in my patient population where I have both difficult-to-control diabetes and difficult-to-control hypertension, there's no doubt that I'm giving that patient a 1-mg overnight dexamethasone suppression test.

I think one point to really draw out here is that this is an inexpensive test. It's relatively easy to do. It's not something that puts the patient in any danger with regard to imaging or getting a big bill, so it's something that we should be able to do on a fairly large level with good effect.

I think the other thing to consider in the big picture is that when we're looking at the modalities with regard to treatment, really the 1-mg overnight dexamethasone suppression test is the test that's designed to be most sensitive. But if you have a patient where the probability is not pushing you in that direction, there are always other tests that you can do to confirm a diagnosis before you make a treatment decision. So although the study was done with the overnight 1-mg dexamethasone suppression test, it was there mostly to prove a hypothesis rather than define an overall treatment modality.

What's the impact with regard to cardiology?

Dr. Plutzky:
Well, I think we're, just at the beginning of this era of recognizing and pushing cardiologists to think about it. I think we're all as providers really interested in root causes, and we see that all the time in cardiology. It's one of the reasons why we've become so invested in LDL control and participated in that research and in implementing that. At one point that really wasn't something that cardiologists thought about that much, and I think it's because of that interest in getting at root causes.

I see hypercortisolism in that same kind of space. I think your comments about that the DST suppression test is not complicated has been an important message. And I think also reinforcing those comments from you is the idea that there's always a spectrum of engagement as these issues start spilling into other areas like cardiology. And it evolves over time. And certainly we've seen that in terms of cardiologists embracing management of diabetes and realizing that there are therapies that improve outcomes.

And so on the far side of the spectrum is simply recognizing and seeing it, and saying this is a patient who really has resistant hypertension or difficult-to-control diabetes. Maybe there's hypercortisolism, and maybe I should have a conversation with the internist about this or even refer them to someone else. That's the far side of the spectrum that comes out of this data.

A step up from that is saying, you know what, I think that data is quite impressive out of CATALYST and MOMENTUM. I'm going to screen, and if it's positive, maybe I'll continue to look for additional tests, as you reference, or maybe that's the point at which I refer. But it's that engagement that I think is important. I think we're starting to see that a lot more in cardiology practices. We have several here at the Brigham and Women's Hospital that I get outreach, having been involved with this research from the nurse practitioners and the PAs who are embracing this and saying, ‘Well, I'm doing a lot of our hypertension management, and so I'm very interested in executing on that.’

So I think it's always exciting in medicine when you're sort of part of that inflection point of a whole new era, and I think that's really where we are here with hypercortisolism. I imagine you probably agree with me that it's really an area that's changing and will continue

to evolve.

Dr. Eilerman:
It's a very exciting time and a really good opportunity to help people that have been really struggling in the past.

Dr. Plutzky:
I want to thank my colleague, Dr. Brad Eilerman, for his participation today. The insights he provided are very helpful, interesting, and informative, certainly for myself and no doubt for everyone participating in the discussion. Thank you, Brad. Look forward to continuing to work with you and to see how this field evolves and this opportunity to really identify causes of disease and cardiovascular disease in patients with hypercortisolism.

Dr. Eilerman:
Thanks for having me.

Announcer:
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