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Continuing the Search: New Data on Hypercortisolism Prevalence in Difficult-to-Control Metabolic Conditions

Announcer:
Welcome to CME on ReachMD. This activity is the third in a series titled, “The Cortisol Reports.” This episode, titled “Continuing the Search: New Data on Hypercortisolism Prevalence in Difficult-to-Control Metabolic Conditions,” is 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. Bhatt:
2024 and 2025 brought us contemporary data on the prevalence of hypercortisolism in people with difficult-to-control cardiometabolic conditions. And now, 2026 has delivered even more new data with more trials ongoing. Let’s dig into these data and what it means for practice.

This is CME on ReachMD, and I’m Dr. Deepak Bhatt. Joining me to discuss hypercortisolism prevalence in people with difficult-to-control metabolic conditions is Dr. Christian Mende. Dr. Mende, thanks for being here today.

Dr. Mende:
Yeah, thank you for inviting me. It’s a pleasure to work with you again. Thank you.

Dr. Bhatt:
So, Dr. Mende, to give us some background, can you talk about the link between hypercortisolism and difficult-to-control cardiometabolic conditions?

Dr. Mende:
Yeah, my pleasure. Hypercortisolism was actually for the first time described about 90 years ago as Cushing’s disease. At that time, the elevation of cortisol was very severe. What we have learned in the last 10, 15 years is that milder or moderate elevations of cortisol play a very important role in cardiorenal syndrome, specifically in conditions such as cardiovascular disease, difficult-to-control hypertension and diabetes, as well as renal disease. So at this point we need to completely rethink that the patients with elevated cortisol levels do not look different from anybody else, and we need to have very high index of suspicion. And if you have somebody with hypertension, particularly refractory hypertension which is difficult to control, or you’re on three medications for diabetes and still have an elevated A1C, or you’re a younger person or have unexplained osteoporosis, these patients today all need to undergo a cortisol suppression test.

So at this point, I would like to ask Dr. Bhatt to give us additional data from his recent presentation at ACC.

Dr. Bhatt:
Well, you’re right. I had recently presented the MOMENTUM study as a late breaker at the American College of Cardiology Annual Sessions, and just to let the audience know what that study was about, we enrolled over 1,000 patients with resistant hypertension. The definition of resistant hypertension is the American Heart Association definition, meeting one of two criteria to count as resistant hypertension. Criterion #1, systolic blood pressure greater than or equal to 130 mm of mercury despite the use of three or more blood

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pressure medicines from different classes at maximally tolerated doses, and one of those classes has to be a diuretic. The other one is a systolic blood pressure at any level with the use of four or more blood pressure medications from different classes.. We managed to get 1,000 patients from around the United States, actually enrolled them very rapidly. It turns out there are a lot of these patients out there. And then what we did was carefully assess for the prevalence of hypercortisolism. That was the primary endpoint of the MOMENTUM study.

And to do that, we carefully measure their cortisol levels. So we used a dexamethasone suppression test, very easy to do. A milligram of dexamethasone is what the patient takes at around 11:00 p.m., say tonight, and then tomorrow at around 8:00 a.m. has their blood drawn for cortisol and dexamethasone. And for the purposes of the study, if the cortisol level was greater than 1.8 mcg/dL and the dexamethasone was greater than or equal to 140 ng/dL, they were categorized as having hypercortisolism, and if not, they were categorized as not having hypercortisolism. The overall prevalence of hypercortisolism, the primary endpoint in this population of patients with true resistant hypertension was 27.3%, so over 1/4 of the patients had hypercortisolism, which is much higher than any one of us actually predicted, those of us involved in the study, so quite eye-opening. A quarter of these patients with hypercortisolism among this cohort with resistant hypertension had adrenal nodules on their CT scans, 24.3%, basically a quarter of patients, so potentially then something that's actionable, something that might lead to surgery, perhaps curative surgery, so useful information from patients undergoing screening.

Now, I'll point out, when we looked at the baseline characteristics of these resistant hypertension patients with or without hypercortisolism, it wasn't really any sort of smoking gun in terms of "Oh yeah, that patient looks like they have hypercortisolism." In fact, the ones with hypercortisolism had lower body mass index and waist circumference than those without hypercortisolism. So these weren't patients, you know, with a buffalo hump or moon faces that are just screaming, "Hey, you know, I have very high cortisol levels." If you didn't look, if you didn't test, you wouldn't find, so that was all very eye-opening. As well, the ones with hypercortisolism tended to have higher rates of things like cardiac disorders, atrial fibrillation, coronary disease, heart failure, more diabetes, worse kidney disease at baseline, more markers of being at risk for progression of kidney disease, so lots of other cardiovascular, cardiometabolic badness that was traveling along with the presence of hypercortisolism.

So the bottom line message, at least the MOMENTUM investigators felt these results point to, is that in patients with resistant hypertension, we really ought to be screening for hypercortisolism.

Dr. Mende:
I think that was the most, the most striking aspect is that actually the, if you look at the endocrine hypertension, that in the literature right now, aldosteronism is always considered to be the most common. And for the first time, I think the numbers were small, but the hypercortisolism actually was more frequent than, than hyperaldosteronism, we now should actually say, "If you look at the aldosterone-to-renin ratio, you should also at the same time absolutely look at that patient and do a cortisol suppression test, because otherwise, you're missing out on a second condition, which is just as common.

I think the primary care—when whoever takes care of patients with hypertension and cardiovascular disease now needs to be aware that, that the patient's appearance does not help you make a diagnosis. If you have particularly difficult-to-control diabetes and you're on two medications or more not controlled, you have difficult-to-control hypertension, the two or more, or even if you're not meeting all the criteria for refractory or resistant hypertension, at that point you need to be aware that hypercortisolism is a very common diagnosis, and uncontrolled diabetes or uncontrolled hypertension actually is as much as one out of three patients who have hypercortisolism. So, why is it so important? Because in addition to the medications, you control blood pressure or, or low albuminuria, or to treat your cardiovascular condition, you need to address the abnormality, which is the elevated cortisol level. So it's not just that you make a diagnosis. I think it will change your therapeutic approach.

Dr. Bhatt:
Yeah, I agree with you about that. I do think, you know, the data from MOMENTUM are actionable and should lead to testing, of course. And not everyone is going to be necessarily familiar with what to do next after that dexamethasone suppression test, but I guess I'd say it's simple to do. You can just have your electronic health record set up, the specific order sets. You don't have to remember the exact doses. Just give the patient a prescription for a milligram of dexamethasone that they'll take at around 11:00 p.m. and then the blood testing the next day. Of course, MOMENTUM—I've presented the data on behalf of the MOMENTUM investigators. The data still do need to be peer reviewed and published and still need that degree of vetting, but it does seem like that prevalence data in a cohort of over 1,000 patients is a really valid and actionable piece of data.

Dr. Mende:
So this is the perspective from my standpoint, and I would like to ask Dr. Bhatt, please tell us what additional studies are on ongoing at this point?

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Dr. Bhatt:
Well, there are other studies, trials going on in this area. For sure, resistant hypertension, hypertension more broadly, has become a really hot area in cardiovascular medicine. There are studies going on to look at different agents to specifically target patients with elevated cortisol that might be contributing to their diabetes that's difficult to control or to their resistant hypertension, or both. There are agents already in use for the purpose of diabetes in association with hypercortisolism and investigations going on to see if there can be specific targeting of therapies in those with resistant hypertension that may be due to hypercortisolism, so I think this will be the really important next step in this journey of hypercortisolism, not just identifying it. That itself is important. Patients are often happy just knowing, "Oh, there's something that may be contributing to causing my resistant hypertension." But the next step in the journey, of course, is specific therapeutics.

We're reaching the end of our program, Dr. Mende. But before we wrap up, what are the key takeaways from our discussion that we want clinicians to remember?

Dr. Mende:
I think we want clinicians to remember that we actually now have missed for decades hypercortisolism, that this is a condition which is much more common, that anybody with difficult-to-control hypertension or difficult to control diabetes on multiple medications, so-called polypharmacy, indeed they have hypercortisolism. That may be for some population as many as 25% or higher. You need to do a cortisol suppression test, and you need to also be aware that anytime you see an incidentaloma, you see a coincidental appearing adrenal nodule, that this needs to be tested, not just for aldosterone, but at the same time also tested and followed up with a cortisol suppression test. So I think the new agenda is that anytime you think about aldosterone, hormonally induced hypertension, or worsened diabetes, that hypercortisolism needs to be on your list of diagnostic studies and on your differential diagnosis.

Dr. Bhatt:
Yeah, I agree with you. That's a beautiful way to sum things up. I do think in patients with resistant hypertension, among the list of things to do, we now really should screen for hypercortisolism. We should also certainly screen for hyperaldosteronism. The hypertension guidelines had already recommended some degree of testing for hyperaldosteronism,

Well, that's a great way to round out our conversation on the latest insights into the prevalence of hypercortisolism in patients with difficult-to-control cardiometabolic conditions. I want to thank my guest, Dr. Christian Mende, for helping us better understand how to use these data in practice to improve care. Dr. Mende, it was great speaking with you today.

Dr. Mende:
It was a pleasure to participate. Thank you.

Announcer:
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