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Keys to Optimizing LDL Levels in Statin-Intolerant Patients

Announcer:
You're listening to *Heart Matters* on ReachMD, and this episode is sponsored by Esperion Therapeutics.

Here's your host, Dr. Charles Turck.

Dr. Turck:
Welcome to *Heart Matters* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss how we can achieve optimal LDL levels in statin-intolerant patients is endocrinologist Dr. Yehuda Handelsman, who's the Medical Director and Principal Investigator at the Metabolic Institute of America. Dr. Handelsman, welcome to the program.

Dr. Handelsman:
Well thank you for having me.

Dr. Turck:
So let's start with some background, Dr. Handelsman. Can you give us an overview of the most common statin-related side effects?

Dr. Handelsman:
Sure. So the main side effect of statins is muscle pain, or rather muscle ache. And I want to differentiate it. It's not if you are playing tennis and your right arm is now painful and therefore, must be the statins. And I hear a lot of that. It's really more of a generalized ache of the muscles in the body up to the point where the patient can't get up from his seat, or can't go ride his bike. So it's this kind of thing. It's just general muscle aches that one would describe as extreme one. But usually it's an ache on the thighs, on the arms, and so on.

Then we have something we call myositis, which is true inflammation of the muscles. We will know that when we check the CPK, which is a measure of muscle breakdown. And if the CPK is up at least 10 to 20 times, we call it myositis, which is not often. It's an infrequent side effect that we're seeing, but it exists.

And worst of all is a condition called rhabdomyolysis, really a true breakdown of the muscles where the CPK can be 40 times or more. This can be a life-threatening condition, but luckily though, it is very rare. But once we stop the medication, it usually stops and it's not there.

Dr. Turck:
And as a quick follow-up to that, how prevalent is statin intolerance?

Dr. Handelsman:
So statin intolerance is quite an interesting look and definition perhaps. The numbers that you will see would say five percent to 30 percent. I think in trials where they look specifically at that and compare it to placebo, we're looking at about the five to 7.5 percent. I don't think it's important. What's more important is what the patient thinks. And the number of patients that think they may have a statin tolerance, whether for real or a perceived one, can be up to 25 or even 30 percent. There is quite a discrepancy between a true statin intolerance versus a perceived statin intolerance.

Dr. Turck:
So with that background in mind, let's turn our attention to the updated consensus statement from the National Lipid Association, or NLA for short. Dr. Handelsman, what do they recommend for reducing LDL in statin intolerant patients?

Dr. Handelsman:
The first position statement for statin intolerance by the NLA was in 2014. And this is now an update, perhaps because we've got a few more medications that we can use in these populations. You see, the FDA at the time did not really accept the concept of statin intolerance. And what they did, and I actually give them a shout-out for that, is actually they call it the most tolerated statin dose that the patient can take. And I thought it was a very interesting way for the FDA, rather than to go into different identifying true statin tolerances, say, 'hey, whatever the patient can tolerate, will accept a statin tolerance.'

What the NLA did in their newer update right now is actually they try to define it in a slightly different way. We always said that in order to have a true statin intolerance, what we have is to try at least two different statins, to stop the statin when they have the side effect, to restart the statin again, perhaps reduce the dose, and then, if not, try another one. The NLA did not divert much away from that; they just added another aspect and say complete statin intolerance if somebody cannot tolerate anything or incomplete statin intolerance. So complete would be tried statin, reduced the dose, usually it's a daily dose, the lowest dose, they define what the lower doses are on the different statins, and see that they cannot take it even daily, then to look at another statins, and perhaps look at alternate mode of taking it, say three times a week or two times a week, and see if people can tolerate it a bit better. So the new thing here is complete statin intolerance versus incomplete that they have on the update.

Dr. Turck:
For those just tuning in, you're listening to *Heart Matters* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Yehuda Handelsman about the latest guidance on reducing LDL levels in statin-intolerant patients.

Now let's zero in on another set of recommendations. Dr. Handelsman, what can you tell us about the ACC Expert Consensus Decision Pathway Guidance on the role of therapies other than statins?

Dr. Handelsman:
So this newer update on non-statin ways to reach LDL goal still goes to explain at length the whole history of statins, when to use statins, and what the 2013 guideline was in the other pathways. And that's to say that we've got some newer stuff right now that today's clinician wants to use. They also kind of put in new targets. They don't go by goal, so it's targets for management, including targets that were introduced in the 2017 guideline by the European Society of Cardiologists. They adopted that in 2019, to look at the LDL goal below 55.

So in the current non-statin pathway, we incorporate different patients, the ACC incorporates different patient scenarios where they show how you can reach patients at a very high risk to get a target of less than a 55 LDL. I have to speak ACC lingo on this one. So I actually liked what they did this time. I think it was a little bit complicated, but at the end of the day, they said we've got a lot of ways we can get today's patients to the correct target, which a lot of patients did not get with statin alone. So statin and non-statin together are a great combination, whether it is ezetimibe or coleselevam that we've had for a long time. Both of them have about 15 to 20 percent reduction on LDL. The PCSK9 inhibitors or the PCSK9 that reduce production, a newer drug was recently introduced in glycerin. You can reduce LDL by about 55 to 60 percent independently on top of statins. So whatever statin dose you can have when you add these drugs it is much better. And then we've got another new drug, bempedoic acid, which also has about a 20 percent impact on the LDL, and it also comes as a combination with ezetimibe, so bempedoic acid/ezetimibe. It's a nice combination because it's a fixed dose. It's a 10 milligram and 180 milligram of this ezetimibe and 180 milligram of bempedoic acid. And together, they get a 38 to 40 percent reduction on or near 40 percent reduction on the LDL. So if it's on top of a statin, it's wonderful. And if it's by itself, it's not too bad, and it looks at different combinations.

Dr. Turck:
And if we look beyond the NLA and ACC recommendations, are there any other management strategies that we can use to achieve optimal LDL levels with reduced side effects?

Dr. Handelsman:
So we have lots of options today. And as I said, we've had guidelines out there that have been recommending usage of combination therapy with statins and non-statins. Or just statins or non-statins. It's quite easy to deal with, it's not a very complicated subject. I think there are some definitions that make it a little bit hard to understand. But in general, you seen an LDL, you identify the risk of the patient, and you try to reduce this LDL based on that patient with no risk. Maybe LDL is at 100, which is moderate risk, and maybe LDL is at a high risk, or at 70 very high risk, or what we like to call extreme risk is less than 55. There is even a recommendation now by a couple groups. One is the European Society of Cardiology and the other one is a group that developed something called diabetes cardiorenal metabolic diseases that suggests that if people have an LDL less than 55 and another event within two years, they maybe should go to an LDL of 40. But there is not enough data on that.

But the interesting thing is we can get people now to almost any LDL that we want. Even a lot of people that have heterozygous FH,

when the LDL start is 200 and above, and that's in combination, we start on the PCSK9, ezetimibe, and bempedoic acid, we can get them to as low as we want. We've never had it before. And that's why I'm happy that a multitude of clinicians have been doing it right now for a while: using combination therapy as early as possible to get people to as low as possible a target based on their risks.

Dr. Turck:
And as that brings us to the end of today's program, I want to thank my guest, Dr. Yehuda Handelsman, for helping us better understand how we can reduce LDL levels in statin intolerant patients. Dr. Handelsman, it was great having you on the program.

Dr. Handelsman:
Thank you for having me. And I really commend you for doing that. It's an important subject.

Announcer:
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