Lipid Management Post ACS or Revas: What Therapies Should be Combined

Announcer: Welcome to the Mayo Clinic Cardiovascular Continuing Medical Education podcast. Join us each week to discuss the most pressing topics in cardiology and gain valuable insights that can be directly applied to your practice.

Dr. Hayes - Welcome back to Mayo Clinic cardiovascular podcast series, "Interviews with the Experts." I'm your host, Sharonne Hayes. I'm a non-invasive cardiologist and vice chair of faculty development and academic advancement for the Department of Cardiovascular Medicine right here in Rochester, Minnesota. Today I'm joined by Dr. Anna Svatikova She is a preventive cardiologist and echocardiographer. Today our topic is lipid management in secondary prevention of cardiovascular disease. So important topic and some people have thought "Well, we're done with that 'cause we've got statins." But in the past year or two there's been so much excitement about some new agents. So we know that statins are the mainstay of treatment of hyperlipidemia is the statin era over with all these new options?

Dr. Svatikova - Yeah, thanks Sharonne, and first of all pleasure to join you on this podcast. It's a great question. So in recent years, new lipid lowering drugs have emerged, as you said, but the statin era is not over. Statins continue to be the first line and the foundation of lipid management for both primary and secondary cardiovascular prevention. We are all very familiar and comfortable with use of statins. They came out in like 1987 in the United States and interestingly they have been also the highest selling drug in the history and the most studied, when we look at randomized clinical trials. Patients with established ASCVD, those that suffered cardiac event or are after revascularization like PCI or CABG should be on maximum tolerated statin dose. We know from studies that statins indeed reduce mortality. What is true however, is that unfortunately in two out of three patients, statins are simply not enough. They continue to have residual cardiovascular risk despite a treatment on statin and we need to lower their LDL further. Also, some patients have statin intolerance and non-statin drugs need to be considered to lower their LDL. So I think that the statin era is not over but statins continue to be the first line therapy. If patients can tolerate it, I say keep going and even less than daily dosing of statin has been shown to be beneficial reducing the LDL by 15, 20%. But simply, if they cannot tolerate it we really have to think about the other agents.

Dr. Hayes - Yeah, so we'll talk about when statins are not enough in a little bit but how common is statin intolerance, really? You know, patients of that age that we are often prescribing statins also have lots of aches and pains and there's been a lot written about the nocebo effect, but when should we really be concerned and how common is it?

Dr. Svatikova - Yeah, great question. So we all see these patients in our clinics. And in general population 10 to 20% of patients have statin intolerance based on observational studies. And 90% of intolerance, as you mentioned Sharonne, is from myalgia. What we need to keep in mind that these myalgias occur bilaterally and patients would say, you know "I have bilateral muscle aches, stiffness, soreness." They can occur after just few weeks of being on statin, but some patients come even years later especially if they had some other big triggers, some surgery or

infection that they started to develop a statin intolerance with myalgias. Other times we have patients in clinic that they come and they say, "Well, I don't want a statin because I'm worried about developing diabetes," right? It is true that impaired fasting glucose and diabetes can develop, but typically it's in patients that have predisposition to diabetes such as patients with metabolic syndrome, it has been shown that actually these patients get diabetes maybe three months earlier when they're on statin as they would otherwise without it. So they get it anyway, but just earlier. One thing to remember is that for every one patient that gets diabetes there are five heart attacks prevented. So we really need to weigh the risks and benefits. I think those are the most common, you know, the myalgia, the diabetes. Some patients come up with, you know, worries about dementia, but the studies do not support that.

Dr. Hayes - Yeah, if anything, the statins support reducing risk of dementia because it's vascular dementia, right?

Dr. Svatikova - Right, yeah.

Dr. Hayes - So why don't you kind of give us an overall summary about some of these newer drugs and where their role is now or perhaps in the future for our patients?

Dr. Svatikova - Yeah, that's a really important question for any provider, whether cardiologists, internal medicine, colleagues. So statins, as I mentioned first, and the other most common drug that we are also very familiar with is as ezetimibe or Zetia, and that's frequently using combination with statin. It has been shown to lower the LDL by about 15 to 20%. So it's a pretty modest reduction, also in cardiovascular risk. It blocks cholesterol absorption in the gut so it works in a different pathway. The other oral agent that is newer is bempedoic acid and it's reserved after generic drugs are used. As I mentioned, it's an oral agent 180 milligrams daily and similarly to Zetia it lowers the LDL by about 20% on top of statins. The FDA approved it for patients that have ASCVD and don't have their LDL at goal. It works upstream from where statins work. Side effects I think that we should be aware of is they may increase uric acid levels so we should be careful when prescribing it or we should not prescribe it in patients that have history of gout. And also the other big one is tendon rupture. So we should, you know, watch out for people if they come with cane or they're limping, you know, did they have any history of recent tendon rupture? Now on the other hand we have the injectable drugs, the PCSK9 inhibitors, evolocumab and alirocumab and they are the monoclonal therapies that were approved in 2015 and they're extremely effective. They lower LDL by 55 to 60%, they bind to PCSK9. They inhibit the, I would say, labeling of the LDL receptor for degradation and therefore their prolonged LDL receptor activity. Patients get them as an injection every two weeks. Inclisiran is the other and the newest on the block from the injectable drugs that was recently approved by the FDA. And similarly it's reserved for patients that have residual ASCVD risks. They are not at LDL goal, they are on maximum tolerated statins and they also reduce the LDL by 55% or so on top of statins. These drugs, however are not self-administered compared to PCSK9 inhibitors. So patients would need to come to their providers and get it injected.

Dr. Hayes - How often is inclisiran?

Dr. Svatikova - Inclisiran, so after the first dose they get a booster at three months and then every six months. So it's only two times a year later on, yeah.

Dr. Hayes - So, I think what you've outlined is we should start thinking about these injectable drugs when side effects of the others or insufficient reaching of goal is there. Are there any other, I mean obviously they are newer require some pre-approval and have some costs which can be a barrier for some patients. Are there any other either side effects or things we need to be talking to our patients before considering those two?

Dr. Svatikova - Yeah, great question. I think the major thing is to be aware of is the cost, that they're not cheap, they need pre-approval, but I think we are working heavily with insurances and they're becoming more and more affordable. The PCSK9 inhibitors are usually well tolerated. Inclisiran recently the side effects, for both of them, have injection side reactions but inclisiran may have bronchitis, diarrhea. But both of these injectable drugs PCSK9 inhibitors or inclisiran still can cause muscle aches but much lesser degree to about like 5% of patients may come with muscle ache.

Dr. Hayes - Okay, so now that we've got these truly powerful drugs that can, you know, cut cholesterol in more than half. We're seeing patients with LDLs of 35 40 really low. So is there a too low for, you know, we've never thought it was too low if somebody naturally had low LDL but we're driving this down with medication. What's the thought on, is there a too low?

Dr. Svatikova - Yeah, great question. Especially now after the 2022 ACC expert consensus guidelines that say that we should drive it, you know, to lower than 55 especially in patients that have had the cardiac event. So how low to go? The opinions differ on this. There does not appear to be a threshold of LDL cholesterol below which benefits cease to exist. Recent studies show that LDL less than 30 milligrams per deciliter shows a significant reduction in cardiovascular death, unstable angina, MI or cardiovascular revascularization compared to those that had LDL over 30. But at the same time, we need to remember that cholesterol does have a role in the body and every cell in our body needs a cholesterol. We need cholesterol to make a cell wall. We need cholesterol to make hormones like estrogen, progesterone, testosterone. So some opinions are that we probably need like 25 or 30 milligrams per deciliter so that our tissues get enough and we just don't know what the long-term side effects are if we drive it so low like below 25 or so. In general, I would say keep the LDL low. There's a lot of benefits with lowering the LDL.

Dr. Hayes - Yeah, are people who, is there evidence that in people who we do drive it low, like maybe less than 30 or 40, do they have more side effects? I have been concerned if I have somebody and they're, I come back after I've started a statin or any other medication and their LDL is less than 30 I might back off on the dose and I don't know if that's right or not. Particularly in young people and I treat a lot of young people with coronary disease.

Dr. Svatikova - Yeah, I agree with you. I think we should take each patient individually and tailor the therapy to them, and especially if they're having some side effects that are, even some mild to moderate, that are limiting their lifestyle especially if they're young, we need to discuss it with them and see how much they can tolerate it or whether we should back off.

Dr. Hayes - We're all excited. It is nice to think that we have some of these new tools that it can somehow make us forget that we have some great old tools, right? The tried and true lifestyle, that we'd been talking about. Now, that was the only thing available 40 years ago. But can you talk, speak to, especially related to lipids, how should we approach this? Patients may come and say, "Hey maybe I can eat, you know, I can eat liver again." or "I can eat all the eggs I want now that you've given me these drugs." So tell us about lifestyle because I think that's an important message perhaps to end on.

Dr. Svatikova - Absolutely, we should never underestimate the power of lifestyle and without healthy lifestyle, all these drugs that we talked about today, whether statins, whether the injectable PCSK9 inhibitors, or other lipid lowering drugs, they become less effective if they are not in combination with lifestyle. Also noted by FDA in their guidelines, you know, lipid lowering medication should be in addition to healthy lifestyle, they are not separate and a pill will never replace healthy lifestyle. So Mediterranean type of diet from multiple studies we know that that's the most heart protective. I typically encourage people to really increase their intake of vegetables and fruits, daily intake. Beans, legumes, fish, white meat, extra virgin olive oil, few nuts per day and focus on eating less dairy, less cheese, less red meat, avoid processed foods, avoid trans fats. And I always say read the labels of all the products or snacks that we get, you know, how much sugar there is, what sort of oils are being used and the more ingredients there are probably the less nutritious that food becomes. Exercise is very important, especially that increases the HDL and lower triglycerides. Our recommendations are to do at least 150 minutes of moderate intensity activity, including intervals. The intervals become very powerful, but the key, especially for the elderly people is not to become sedentary. I think that's the most important when we talk to patients about diet and exercise. The other important things are, you know, sleep, getting healthy sleep and stress reduction.

Dr. Hayes - Yeah, I think I focus on exercise a lot because I think, and I emphasize it, because exercise by itself is unlikely to significantly reduce cholesterol, right? That should not be the goal, and people have been disappointed because somehow, you know their HDL went from 35 to 36 and they've been working out, you know, two hours a day. And so to adjust expectations is recognizing that exercise does so many other things. You know, maintains weight, helps the stress and all of those things. And people kind of, I think if we focus too much on some of these, on actually the numbers, they give up, and so I think just talking about the whole package.

Dr. Svatikova - Yeah.

Dr. Hayes - I like, your drugs won't work unless you do this.

Dr. Svatikova - That's right, yeah.

Dr. Hayes - So this has been a great topic because I think we've got some exciting new tools for lipid lowering and particularly for our folks who already have, so for secondary prevention of coronary disease. So thank you so much. This wraps up this week's episode of "Interviews With the Experts," and I'd really like to thank Dr. Svatikova for joining me today and discussing this important topic. We look forward to joining you again next week for another interview with the expert, be well.

Dr. Svatikova - Thank you, my pleasure Sharonne, thank you for having me.