

Easy Management of Statin induced Myalgias

Transcript Details

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Dr. Domino:

Welcome, you're listening to Pri-Med's podcast series, Frankly Speaking, and I am your host, Frank Domino. I'm a family physician at the University of Massachusetts Medical School in Worcester and joining me today is Robert Baldor. Bob is the Senior Vice Chair in the Department of Family Medicine & Community Health here at the University of Massachusetts. Welcome, Bob.

Dr. Baldor:

Thanks, Frank. I know, typically, you're running these pods and trying to learn from your colleagues and today I really am thrilled because I understand you're gonna give us a little bit of an overview of what's going on here in the world of lipids. And so, I thought if you could help us think through some of this as to what's new in some of the latest guidelines around lipid management, testing, and I know that there's different criteria on who should be on what kind of lipids and high and low densities. It'd be really great if you could help walk us through that. And then, finally, these new agents out there, the PCSK9 inhibitors, I don't understand them. If you can help me and help my colleagues figure this out, that would be great.

Dr. Domino:

Sure thing, Bob. In 2013, the American Heart Association published new guidelines and, for the most part, had us turn away from using LDLs as a diagnostic and treatment parameter. And they said there's really only four groups of folks who need cholesterol treatment. And those are folks with known heart disease, and we used to call it atherosclerotic or coronary artery disease, now we call it ischemic heart disease. Anyone who's had a cardiac event of any sort, they should

probably be on a statin. The other populations are anyone with an LDL over 190, so that's the only LDL parameter we, in primary care, need to worry about. So we're still measuring LDLs. We're still be filing the LDLs. You don't have to get fasting LDL cholesterol levels anymore. You can use non-fasting levels. But an LDL over 190 implies some familial disorder and those folks probably would benefit from statins.

The third group are diabetics who are between age 40 and 75 who have some degree of cardiovascular risk. And one parameter that people sometimes suggest is an LDL that's less than 190 because then they'd fall on that other category. But a diabetic who's between those two age ranges, 40 and 75, will likely benefit from some intervention with a cholesterol-lowering agent. Now, people sometimes say, "Gee, we're seeing an increased population of diabetes before age 70, and what about all those folks after age 75?" They may benefit. We just don't have any data that supports that. And then the last group, and it's probably the biggest group we see in primary care, is anyone between 40 and 75 who does not have diabetes but has a 10-year risk of a cardiovascular event of about 7.5%.

Dr. Baldor:

And how would we figure that one out?

Dr. Domino:

And the only way to figure that one out is to use a risk calculator and there's a great deal of controversy around risk calculators. I continue to use the American Heart Association's risk calculator. I have one on my phone. When I discuss lipid results with a patient, I pull it up, I plug in the few bits of data that they wanna know: Systolic blood pressure, gender, age, and total on HDL cholesterol. They do not use, in that calculation, LDL cholesterol, just total on HDL. And based upon that, I'll get a percent risk of cardiovascular events in the next 10 years. And I talk to patients. Patients are very worried about heart disease. They have a strong family history of premature, early heart disease. Folks who have a lot of anxiety about it, I'm willing to entertain a statin, a moderate-intensity statin between 5 and 7.5.

Dr. Baldor:

So it's 5 and 7.5 at 10-year risk of developing a cardiac event?

Dr. Domino:

Correct. And over 7.5, I certainly talk more aggressively about statin use. I do have a subset of patients who refuse to take statins and that's mostly because they've read about some of the fears associated with statin use, including the myalgias and the possible increased risk in diabetes. And if someone is truly resistant to statins and their risk is over 7.5, I tell them the very best way to lower that risk is to look at risk factors. And smoking, of course, is probably the hugest risk factor that they can change. And if they can't change that, they can raise their HDL through exercise. The only way we've ever seen HDL raising impact cardiovascular outcomes is improving through exercise.

Dr. Baldor:

What about red wine? I have really buffed up my supply at home because I thought that was gonna help me.

Dr. Domino:

Red wine may help you for many reasons, Bob, but I'm not sure it's gonna improve your HDL or improve it to the point where it's gonna improve cardiac outcomes.

Dr. Baldor:

I gotta continue to delude myself in that.

Dr. Domino:

You can continue to do so. So that's the current guidelines. I think they're pretty straightforward. There are concerns, a great deal, about the adverse effects of statins. And there is a small but appreciable increase in risk for patients taking statins for more than a few years, on the

development of type 2 diabetes. And we don't know why, we don't know who's at risk or maybe the physiology that's getting you hyperlipidemic is also putting you at risk for diabetes, much like we think goes on with metabolic syndrome. So I think you can use those parameters. These are guidelines, they're not requirements, and you should tailor your care to patients' needs and what you think is best for them. So if you've got a patient who isn't exercising and smokes a pack and a half cigarettes a day, and has poorly-controlled high blood pressure, and they're interested in taking a statin to mitigate their risk, you need to help them recognize that unless they change some of their other risk factors, they're probably just taking a pill and having a very, very small impact on the prevention of heart disease.

Dr. Baldor:

Okay. Yeah, that's a lot of my patients. So I do wanna touch upon... I've been hearing a lot in the news about statin intolerance. And so we've got patients that are on statin and worried about the side effects. Can you talk more about what the data and literature shows us about that issue?

Dr. Domino:

Well, you know, Bob, this is really where I've been paying quite a bit of attention of late. A paper came out a couple of years ago and I totally missed it. And I was hearing a cardiologist...

Dr. Baldor:

Wait a minute, you missed a paper that came out a couple years ago?

Dr. Domino:

That was about this issue that was truly impactful. So I was in a lecture just a few weeks ago, and a cardiologist was talking about folks who were statin intolerant. And he offhandedly said, "Well, if they can't tolerate a moderate or high-intensity statin every day, have them take it on a non-daily basis, every other day, or even every third day, and you'll still get more bang for your buck than them not taking it at all."

Dr. Baldor:

Is there evidence to support that?

Dr. Domino:

So, being me, I went and looked. And sure enough, I found a number of papers that talk about how to address statin intolerance. And one of my other areas of interest, as you know, Bob, is Vitamin D deficiency. And that's the...

Dr. Baldor:

Oh no, don't tell me Vitamin D factors in here.

Dr. Domino:

I could not believe this. I was unaware of this, but there's actually a fair bit of data that shows if you develop myalgias or myositis associated with statin use, treating Vitamin D deficiency turns out to totally mitigate it in about 85% of patients. I have no idea why, and I can't tell you that I've ever even employed this as a method with patients, but I'm going to start. If someone can't tolerate a statin, I'm gonna aggressively look at their Vitamin D status and replace them and see if things improve.

The other area that they thought we missed in primary care commonly was that if a patient had a great deal of difficulty with tolerating statins was to make sure their thyroid function was adequate, because hypothyroidism, it turns out, tends to play a role in statin intolerance, and not addressing it can be a factor.

The third area, and like I said, the one that was most startling to me, was not using a statin on a daily basis. So think about our really two strongest statins, many patients develop complaints with their use. Atorvastatin has been around quite a bit longer and we know that folks have had trouble tolerating it on a daily basis. But the drugs apparently have a long physiologic half-life. Their influence on parameters that we can measure appears to go well beyond 24 hours. So the

literature, looking at 2013, a great paper came out that did a review, not a systematic review, but did an in-depth review of any publications within MEDLINE on how to use statins on a non-daily basis and their outcomes. And it turns out that if you take the drug every other day, you can still get up to about 38% reduction in LDLs.

Dr. Baldor:

Wow, that's really good.

Dr. Domino:

It really is. And this study looked at anywhere from every other day till once a week. So you can still have a significant impact on patients' cardiovascular risk by using them on a non-daily basis. Taken a step further, we know that for the two high-intensity statins, their costs are quite high. And if you're paying out of pocket on a daily basis for these drugs, you can spend anywhere between \$3 and \$500 a month. Whereas if you're taking them every other day, or every third day, you've cut that cost in half or by up to 70%. So there seems to be some data that supports that as an approach. Now, I'm not saying that this should be our first approach, but I'm saying for folks, especially for those who have cardiac risk factors but do not have known heart disease, this is a very very reasonable approach. It leads to less adverse clinical symptoms and still pretty significant patient outcomes. So I think these two papers tell me a great deal about where we should be going.

Dr. Baldor:

That's terrific. So what about the PCSK9 agents?

Dr. Domino:

So the PS, PC, so this P...

[laughter]

Dr. Baldor:

You go ahead and say that.

Dr. Domino:

Bob, that's such a terrific question. Thank you for raising the issue of the PCSK9 inhibitors. These drugs were just approved by the FDA in 2016, and they've been around actually and studied for quite a few years prior. So I found a recent systematic review on them and, sure enough, they have a very significant impact on LDL lowering. And there's wonderful data that shows they're relatively safe. They are an injection, so they have to be given subcutaneously on a fairly regular basis, but you can get upwards of 30% to 70% reductions in LDLs.

Dr. Baldor:

Well, what about outcomes that we care about? For a lot of times, we've talked about trying to be more patient-centered with our outcomes, reducing cardiovascular events, and so on, not just lowering LDL. Do we have data on that?

Dr. Domino:

Sure, we have absolutely no data on that. So there's no data that currently has been demonstrated to lead to improved cardiovascular events. Now, they're studying it, and I assure you that as soon as that data's available, it'll be published. But right now, even though these drugs have been around for more than a few years, we don't have good patient outcome data to show lower rates of cardiac events, lower rates of cardiac mortality, lower rates of stroke. So...

Dr. Baldor:

We do know it significantly lowers LDL and is a proxy that should have an effect, but we don't know that for sure.

Dr. Domino:

Well, there's a fair bit of arguing amongst the cardiovascular folks about whether LDL is actually a

reasonable proxy. So interestingly, we know that with statin use, LDLs can be used as a proxy. But the question that some folks say is that, "Is there some special effect of statins interrupting the HMG-CoA reductase pathway that is leading to both a lower LDL and a lower cardiovascular risk?" And some folks believe that these newer agents don't work through that pathway, and may not get the same benefit.

So I think the story is still out on those. The only patients I see those being beneficial for in today's world are patients with known heart disease whose LDL is resistant to high-intensity statin or someone with known severe heart disease who has a great deal of trouble tolerating a statin. In those... That latter case, I think it would make perfectly good sense to try a non-daily dose of a high-intensity statin, and then add one of these newer agents in working with a cardiologist who feels comfortable. But I think the use of these drugs, in our current world, is going to remain quite limited until we have a fair bit of data.

One last point on these agents, and I think it's really interesting to note that there have been some cost-effectiveness trials on these drugs. And it's really quite interesting to think about how they had to be used to receive one patient outcome based upon prediction models, not based on true outcome data. So they looked at what they would consider the possibility of a major adverse cardiovascular event and their use, and if the LDL model we typically use with statins holds true, the cost of running one major adverse coronary event is around 2 million. To prevent one death, it's around 8.7 million.

Dr. Baldor:

Wow. So typically, we talk about 100,000 per added year of life as a marker within that. So I mean this sort of leads to that whole discussion that we've been having around the cost of medicines and where we're going with some of these. So hopefully, this will be a benefit for some people and come down as we move forward.

Dr. Domino:

So we used to talk around 50,000 for quality-adjusted life-year, and then we've raised that to 100. You're absolutely right, in just recent years, and one of the big factors was around the management of hepatitis C, which we believe, with the newer agents, runs around \$85,000 a year. This is quite a bit more. So keep in mind, these are interesting meds, they have no outcomes that we think are clinically known at this time, and that their cost makes them very cost-prohibitive.

So I have one patient who is on one of these agents, certainly started by the cardiologist. What upsets me most is that this patient continues to smoke, and has no desire to quit smoking. So my suspicion is this is a great deal of money being spent on an individual that may not necessarily benefit. But till then, I think we have a really good idea about when to use a statin, how to use a statin, how to use a risk calculator. And for patients who are statin-intolerant, try a non-daily dose of those statins to see if you'll improve outcomes.

Dr. Baldor:

Well, that's great, Frank. So obviously, these newer agents, so it's not something I'm gonna be using in my primary care office. And I can't imagine what the PA, prior authorization, must be to go through to get this approved with those costs. So this has been great. So just to summarize here, did a nice job helping us really think about the idea that prescribing statins and lipid-lowering agents should be based on some new classifications for individuals' risk. For people who don't fall into those high-risk categories, use a risk calculator, and then figure out where they fall within that.

If somebody does need a statin, and they're having some problems with intolerance, check a vitamin D level, check a thyroid level, think about using an every-other-day therapy for it to address your needs. This has really been very helpful for me. And the vitamin D thing, I keep going back and forth on is we need to see that crop back up here. Thanks a lot, Frank. And thanks for letting me host the show today on Frankly Speaking.

Dr. Domino:

Thank you, Bob, and have a great day.