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Statin Intolerance: Keys to Patient Counseling and Guidance

Dr. Alan Brown:
You're listening to ReachMD and this is Lipid Luminations sponsored by the National Lipid Association. I'm your host Dr. Alan Brown and with me today is Dr. John Guyton who is an Associate Professor of Medicine and Assistant Professor of Pathology in the Division of Medicine, Endocrinology, and Metabolism at Duke University, School of Medicine. John, thank you very much for taking time to talk with us today.

Dr. John Guyton:
Good to be here, Alan.

Dr. Alan Brown:
So today, we're going to talk about statin safety and we're at the Indianapolis NLA meeting. I had the privilege of hearing your talk at the introduction of the meeting, which I thought was fascinating and I'd like the rest of our audience to get a chance to hear some of your thoughts on statin safety.

As you know, one of the big barriers over the years going back to Lovastatin was this fear of potential toxicity from statins and as time has gone by, the data looks better and better and better but both patients and physicians are still somewhat wary about statin usage. So I'm wondering if you could put into perspective that document that you put together with the NLA on statin safety and tell us a little bit about where we are in 2014 on safety, side effects, et cetera of statins.

Dr. John Guyton:
The report is the second edition of the Statin Safety Task Force. The original Statin Safety Task Force of the National Lipid Association was in 2006. This is the second edition in 2014. I had the good fortune of participating in both of them and this one really changes the focus from safety of statins over to statin intolerance. Statins are extraordinarily safe, but statins are not always tolerated and the risk of permanent organ damage or death from statins is very, very low.

They're just about the safest medications that we have...certainly safer than aspirin, for example, but with regard to statin tolerance, there are reports, a quite good report from France several years ago that ten percent of people taking moderately high doses of statins or high doses of statins will report muscle side effects, myalgia, fatigue. Another report commissioned by the National Lipid Association, I wouldn't call it an internet study, but it was people who were connected to the internet or who were able to use the internet, and that study reported that it's more than one out of four patients taking statins might report myalgia.

We don't really know how many and how many of those people if they were given a blinded pill that was either a statin or how many of them would be able to tell the difference. It might really be more like five percent of people, but even five percent, given the huge number of people for whom statins are recommended in the United States today, even five percent is just a lot of people. They're safe taking the statin but they're not always going to be able to take it because they could be miserable.

Dr. Alan Brown:
I was really fascinated by your presentation looking at sort of _____ (2:54) Dr. Rosenson's discussion of China come up with some sort of scoring system because as a practitioner, people come in with all kinds of complaints and they tend to blame it always on the statin and then trying to determine what really is a statin side effect and what isn't.

So I'm going to ask you to start with what are the types of side effects that one should attribute to a statin. Many doctors order CPK's and if they're normal they discount that the muscle symptoms aren't related to the statin. We know that is not correct. So tell us what typical

statin side effects are that might lead to intolerance and how the practicing physician should deal with that.

Dr. John Guyton:
I'm going to change your question just a little bit.

Dr. Alan Brown:
And I'm going to allow to because I have great respect for you.

Dr. John Guyton:
I'm going to change the question to say who is going to attribute that side effect to the statin and I think the true answer is that it's a partnership and the patient has the final say. That the doctor, or the nurse practitioner, or the provider is really advising the patient in this case, but the patient has the final say and for the individual case, the best data comes from the patient. Only the patient understands what they're truly feeling.

Now, when I'm advising patients, what I'm going to tell them is that if they're getting side effects that are just on one side, if they're getting something that oh, it's just a pain in my left calf and it's sort of right behind the knee, well that might be a joint problem. Maybe joint fluid leaking into the muscle or something like that, but if it's on both sides, if it's in the thighs especially if they can't rise up. Really what makes the difference, is the patient able to go through the day and do the things that they usually do. Is the patient able to get to sleep and we've had instances where statin side effects can interfere just because of aching muscles with sleep.

Is the patient able to do the amount of exercise they need to do? Statin muscle reactions can interact with exercise. Elite athletes who are stressing their muscle to the max have more difficulty taking statins. That's very clear. So is the patient able to get the exercise that we want them to get. Does it interfere with daily activities? And that's where we draw the line. It's not whether they have a little bit of stiffness in the morning, takes an hour or two to really get into the day, but after that, they're fine through the day. That might or might not be due to the statin, but even if it's due to the statin, the statin is going to be doing them so much good that in terms of preventing heart attack and stroke that we would generally think a reasonable person would want to stay on the drug. Those are the main things.

Dr. Alan Brown:
So I guess that comes down to the risk benefit ratio of putting people on the medications. You said as many as 25 percent of people could have side effects. So with an individual patient whose complaining of side effects, you do look at the benefit versus the risk and in that individual you have to make a judgment.

Dr. John Guyton:
Absolutely. Working with the patient, the other name for it is patient-centered medicine, shared decision making, but in this case, the patient is the one who says does the patient have statin intolerance. We know that if we do randomized clinical trials and one of the shocking things about this and I think I understand how it happened, one of the shocking things is we don't have the really good scientific evidence on how often that side effects are truly attributable to the patients. We've had estimates as high as almost 30 percent, estimates as low as one or two percent. I sort of suspect that somewhere in the five percent range where it's truly attributable to the statin, but that's not the question to ask in clinical practice.

The question to ask in clinical practice okay, it might be due to the statin but how bothersome is it, how much does it bother you, and a lot of people, once they think about it, I can do everything I wanted to do anyway and it's not like having an allergy to penicillin or something like that where you know you have a drug side effect or a drug. We shouldn't even call it an allergy. It's a reaction.

Dr. Alan Brown:
All right. So with that said, let's talk briefly about what you do then when a patient comes in and says ‘Doctor, I'm not feeling well. I'm having muscle aches on the medication' and they're convinced it's the medication. What's your approach to the patient for our nonlipidologists in the audience?

Dr. John Guyton:
First of all, if the patient says the patient is convinced that it's due to the medication then that patient is not likely to take the statin, not likely to want to do that. My first response is that I personally am going to still try to use the statin, but I'm going to use either another statin at a fairly low dose or use the same statin but cut the dose down four times, fourfold. I'm not going to just back off by a half. I'm going to cut it down fourfold because I really want to get the dose down to a dose that I think the _____ (7:44). These muscle side effects really are dose dependent and often a regimen that I find most people who report this kind of thing can take. It would be something like atorvastatin, half of the ten-milligram tablet, just five milligrams, Monday, Wednesday, Friday. I'm going down that low. We think that we're still getting 25 to 26 percent LDL cholesterol lowering and the reduction in risk is really proportionate to the LDL

lowering, the reduction in heart attack and stroke risk is really proportionate to the LDL lowering.

Dr. Alan Brown:
If you're just tuning in, you're listening to ReachMD. I'm your host Dr. Alan Brown and today I'm speaking with the famous Dr. John Guyton about statin intolerance. So John, with that said, do you have the patient stop their statin for a while to make sure that the side effects go away or do you just go to a lower dose and if you do stop it, how long should you wait before you might say I'm not sure the statin caused this because the symptoms are persistent.

Dr. John Guyton:
Probably 50/50 with the individual patients. If the side effect is not very strong but the patient really indicates they're not going to stay on this dose of the statin, but they're willing to decrease the dose, we're going to do it that way and sometimes I'll go down and I'll say okay, atorvastatin, five milligrams, twice a week. If you feel fine after that, go up to three times a week. Come back, let's have another discussion in ten weeks or so, eight to twelve weeks, and let's see where we are, but in other people, we're going to stop the statin for at least two weeks, three weeks, four weeks, and then maybe try getting them back on this lower dose or maybe switching to other medications.

Dr. Alan Brown:
I get to quote my experience now that I'm getting old. Usually I'd say within seven to 14 to days, the symptoms resolve completely and it isn't subtle. So in those people who've had difficulty going up the stairs where they really had significant myopathy, and they were weak and felt miserable and we've all had those.

Dr. John Guyton:
I remember a lady who was sitting in the chair and I said okay, hold your hands up in the air and get out of the chair and she just broke down in tears because she couldn't do it and doctors kept telling her to stay on the statins, stay on the statin. I said this is okay. You get off of it. We need to get your strength back and then treat your cholesterol.

Dr. Alan Brown:
And so she probably felt like a completely new person in a week or two, right?

Dr. John Guyton:
Absolutely. Absolutely.

Dr. Alan Brown:
You know, I've had the personal experience of being a _____ (10:00). I grabbed some samples of a statin, took them out of my office and just thought I should be on them and after a month or two months, I just felt like something was terribly wrong with me actually. I got very nervous about it and it was in my office while I was explaining statin side effects to a patient and trying to decide if they had it and then it dawned on me that what an idiot I was that my symptoms were from a statin. So I stopped them and roughly a week later I felt completely like I had gained a few years on my life. So I'm a firm believer in this, but my experience has been you stop it for one to two weeks. In the patients who tell they're not sure if they feel better, that my gut feeling is that probably wasn't the statin. The ones who have statin side effects usually feel remarkably better. Don't you agree within a couple of weeks?

Dr. John Guyton:
Generally so. I'm not sure I'm going to be able to convince that other patient sometimes to take a full dose of a statin but I can usually convince them to take a lower dose.

Dr. Alan Brown:
Yeah. That's great.

Dr. John Guyton:
I'd like to mention another side effect because this comes up fairly frequently and I think it's real but it's much less common. It's a fairly rare and that's the cognitive problems that people can sometimes have with statins. I actually took care of one patient who was a PhD scientist who ultimately died of coronary heart disease, who developed amnesia when he took statins. We could not get him on it. We tried other medications but ultimately it was just too much.

I had a lady who was a doctor's wife, a nurse, very well trained, very articulate woman. She was watching TV with her husband. She had the remote control of the TV in her hand and she turned to her husband and said ‘How do you work this?' She couldn't remember how to change the channel using the TV remote control.

Dr. Alan Brown:

Yeah. So let's put that in to perspective because I've had a similar experience. I had a physicist that was very credible and he was struggling with math, with doing his math when he was on the statin. I had no reason not to believe that this was a real effect. So in the clinical trials, it doesn't seem to be reproducible that you could predict that a percentage of patients are going to get cognitive difficulties but there are these sporadic reports and I've always wondered, do you think there maybe some genetic predisposition that we're not aware of where certain people are just predisposed to cognitive issues with statins, but it's not predictable across the ____ (12:12).

Dr. John Guyton:
Absolutely. It's bound to be genetic. I think it's probably going to be 30 or 40 years before we understand some of the issues into genetics. One of the things in genetics of statin...let me just say I think this is at least ten times less and perhaps 50 times less frequent than the muscle reactions. In our own experience with statin side effects, we're trying to determine what the relative frequency. How many of these patients have muscle problems that are referred? How many of them have cognitive? I think the difference is ten to one or less with regard to the muscle side effects.

We do know that some of the genes that affect statin and tolerance have to do with how the liver takes up the statin because only five percent of that statin actually gets past the liver. You know you absorb it in the gut, but all the blood flow from the gut goes through the liver. How much of it actually gets out to the rest of the body? Five percent or less, but in some people, it's probably 15 percent. In this one genetic test that can be done we rarely, rarely do it. I've done it two or three times that can look at one particular gene present probably in more than 25 percent of the population that can affect that.

Dr. Alan Brown:
That's really interesting and it does help. People don't realize that actually family members can have the same sort of statin intolerance. It does sometimes run in families and someone will tell you my mother couldn't take it either.

Dr. John Guyton:
Oh yeah. Oh yeah.

Dr. Alan Brown:
We used to say that's crazy but it turns out that these kind of genetic enzyme abnormalities can run in families.

Dr. John Guyton:
That's true. Yeah, if there's a family history.

Dr. Alan Brown:
So the last question and you know I could talk to you about this all day and I'm sure the audience would love to hear about it all day, anything to supplements and things that try and reduce statin intolerance. Coenzyme Q10 issue comes up constantly. Some people talk about Vitamin D supplementation. What's the current state of evidence that any of those interventions make a difference in statin intolerance?

Dr. John Guyton:
I don't recommend them. I don't. I never recommend them to patients. I don't think the evidence is there. They might have small effects but I don't think there's sufficient evidence to recommend them. There are some research trials. I want to just touch on one other issue and that's there probably is a bit of an increased risk of diabetes taking statins. To me, that is more of a safety issue than a tolerance issue because if you get diabetes, you've lost beta cells and you're never going to get them back. The beta cells are the cells that produce insulin but the risk associated with taking a statin is worth about two pounds of weight loss. So if the patient can just get their weight down a little bit, you take away the risk associated with the statin and the benefit of reduced heart attacks and strokes which is the main problem with diabetes at least Type 2 diabetes anyway. That's going to be better with a statin.

Dr. Alan Brown:
I'm glad you brought that up. I think our audience needs to know that it's the pre-diabetics that are the ones that seem to be predisposed to more. They already have risk factors for diabetes and that those patients who don't have any risks for diabetes don't seem to be...

Dr. John Guyton:
That's a really good point. Yeah.

Dr. Alan Brown:
Great. Well, terrific. Thank you very much, John, for your insights. I wish we could talk about this more. We probably should do a whole show on the diabetes issue. I think there's plenty to talk about there and some subtleties but you've given us some great insights on how to deal with statin intolerance and the bottom line is when the patient complains, you have to address it.

Dr. John Guyton:

You have to listen to the patient.

Dr. Alan Brown:
Absolutely. I'm your host Dr. Alan Brown. You've been listening to Lipid Luminations sponsored by the National Lipid Association on ReachMD. If you missed any part of this discussion, please visit us at ReachMD dot com slash Lipids to download this podcast and others in the series. Thank you very much Dr. Guyton for joining us, and thank you all for listening.