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Assessing Advancements in Preventative Cardiology

Dr. Sorrentino:
Since the introduction of statin medications in the late 1980s, prevention has become a major focus for cardiology to reduce the burden of cardiovascular disease. Major advancements in prevention have brought about significant changes in how cardiologists treat their patients.

This is Heart Matters on ReachMD, I'm Dr. Matthew Sorrentino, and today it is my pleasure to discuss the field of preventive cardiology with my colleague in prevention, Dr. Alan Brown. Alan, welcome to the program, and would you like to introduce yourself to our audience?

Dr. Brown:
Sure. Thank you, Matt. I am Chief of Cardiology at Advocate Lutheran General Hospital, which is a teaching hospital associated with Advocate Aurora Health in North Western suburbs of Chicago and the National Lipid Association.

Dr. Sorrentino:
Great. Thanks for joining us and allowing me to pick your brain about prevention. We know that after there was a clear understanding of the role that cholesterol played in cardiovascular disease, many preventive groups formed their own specialized lipid clinics and I know at one point, you had a lipid clinic and you used to teach courses to have other physicians learn how to establish their own lipid clinics. But statins made everybody a lipidologist, so is there still a role for lipid clinics in today's day and age?

Dr. Brown:
Yeah, I started a lipid clinic in the mid-1980s and have been running it ever since. Early on, we would get referrals to the lipid clinic for just high cholesterol because folks didn't really know what to do and it is true that with the wide variety of statins, some of which have very good potency. there are fewer patients being referred for just high cholesterol. But a whole new opportunity arose, which was statin-intolerance and a large percentage of people get referred to the lipid clinic because they can't tolerate one or several statins and the average doctor's not exactly sure what to do next. And then secondly, we focus on what I call the top of the pyramid of patients with this lipidemia, which are those folks with clear-cut genetic lipid disorders who have much more severe abnormalities than the average patient, even with atherosclerosis, so I'm referring to people with familial hypercholesterolemia, which though it's the most common autosomal-dominant inherited disorder and occurs in 1 in 250 people, still about 90% of those patients are not properly diagnosed because most physicians are unaware of the illness and the implications. And then we also see the severe hypertriglyceridemia patients, like familial chylomicronemia syndrome patients who have recurrent pancreatitis and generally don't respond well to traditional therapy, as well as other more rare genetic lipid disorders, so we've moved from kind of taking care of everybody who had cholesterol elevation which the average physician is now managing in their practice to those patients with intolerance to drug therapy or those patients who are much more severe due to underlying genetic disorders.

Dr. Sorrentino:
You mentioned familial hypercholesterolemia as one of the more common genetic causes of high cholesterol, I have a sense that this still remains markedly under-diagnosed. Why do you think that's the case and for our audience, what is a screen to try to identify these patients?

Dr. Brown:
So familial hypercholesterolemia, at the least the heterozygous form, occurs in about 1 in 250 patients and it's due to inheriting a bad gene for most commonly, the LDL receptors, so you get a good gene from one parent, a bad gene from the other and half of your LDL receptors on the liver don't work, which leads to halving of the ability of clearing LDL from the blood, so cutting that clearance rate in half

and secondarily leading to doubling of the LDL levels in the blood. So patients with familial hypercholesterolemia usually have LDLs well over 190. There are other causes of having LDL that high but, the higher the LDL is over 190, the more likely it is due to familial hypercholesterolemia. And there are other clinical clues that the patient may have that autosomal dominant disorder because it is a dominant disorder, usually, a first-order relative has similar very high LDL cholesterol, either mom or dad, or brother or sister. There's usually premature heart disease in the family. And about a third of patients will actually have xanthomas, either on the knuckles of their hands or on their Achilles tendons, which is pretty much pathognomonic for the disorder. And if they do carry that genetic mutation, they have 22 times the risk of a cardiovascular event compared to the average individual. If they have high LDL without the mutation, their risk is 6 times the average which is still pretty high, but the thought is that FH patients have such a high risk because their LDL cholesterol is high from birth. So, what docs have to know, and I've had this discussion over the years, they say, "Well, why do I need to know about familial hypercholesterolemia? If someone's LDL is over 250 I'm gonna treat it." And the reason they have to know is because 50% of the children may have heart attacks because nobody recognized that after seeing their parents' lipid levels that the children need to be screened at a very young age. So, I think the key things are to note the disorder so that you initiate cascade screening of the families and you don't miss brothers, sisters, or children and we now start treating the kids when they're about 7 to 8 years old, so it's very important to screen them. I will say that as much as we bash the pharmaceutical industry several new medications have come out that are indicated for FH such as the PCSK9 inhibitors and more recently, bempedoic acid, and all those companies have done massive education on their products, which have included education on familial hypercholesterolemia. So, I think, actually, that's been a good service because I think more doctors have learned about the disorder just from the education from these pharmaceutical companies.

Dr. Sorrentino:
I was gonna ask you about the PCSK9s, they've been out for a while now. What is your impression of the use of these agents for FH and also for other high-risk patients? Have these medicines been well adopted by the field or are they still only being seen by yourself, like in lipid clinics where they're being used?

Dr. Brown:
Yeah, I think that really varies depending on region of the country. We certainly within our healthcare system have not limited the use of PCSK9 inhibitors to just even cardiologists, much less lipidologists, but we've sat down fairly concise indications for which patients should get them. And as you well know, the price has come down pretty dramatically, about 60% since they were originally on the market, so it's easier to get the prescriptions filled without going through a lot of prior authorization. But they are an amazing tool; they lower LDL about 60% on top of whatever we can throw at patients, so once you've got them on the statin, once you have them on ezetimibe, you can still get an additional almost 60% LDL-lowering adding a PCSK9 inhibitor. And they have the advantage of very few side effects and no drug interactions because they're basically an antibody, so they've been extremely valuable. I do think that there are lots of patients who would benefit from them, not just patients with familial hypercholesterolemia, but patients with atherosclerosis who have either been intolerant to statins or have had inadequate LDL lowering on statins and we do have to continue to expand their use while we're waiting for some newer agents that are gonna be out soon that may have some advantages in terms of the amount of dosing.

Dr. Sorrentino:
I think it's been remarkable the LDL-reduction we can get with this type of combination therapy. I remember years ago that if your statin didn't get you to goal and you had somebody with a markedly high LDL, we had to consider LDL apheresis; now I suspect this isn't done very much. Is there any role for LDL apheresis, or is that only the rare homozygote patient that we might need to consider that type of therapy?

Dr. Brown:
That's another great question. So, it is true that many of the apheresis centers around the country were doing apheresis on severe heterozygous FH patients. As you know, the homozygous patient almost always need to, at least initially, be on apheresis, which is similar to dialysis, a method of removing the blood and then running it through a filter that removes the LDL cholesterol and then passing it back into the blood. But because of the PCSK9 inhibitors, a lot of people that were on apheresis for heterozygous FH no longer need it. What has been happening in those pheresis centers that are still quite active, however, is pherising for LP(a) and the reason that's being done is, though the science is not fantastic, there've been 2 or 3 studies showing that in patients that are having recurrent coronary events, despite good control of their LDLs, but who have very high LP(a)s that they seem to have fewer events after being placed on apheresis to remove the LP(a) and those studies when I say they're not perfect science, they're not randomized prospective placebo-controlled trials; patients are serving as their own control, so they look at how many times did they get admitted for cardiac event the several years before they went on apheresis versus the several years after, and the studies look like there was a significant decrease in recurrent cardiac events. Also, as I'm sure you know, Matt, PCSK9 inhibitors, on average, can lower LP(a) about 30%; it is

a little bit variable from one patient to another, but in looking at the outcome trials with PCSK9 inhibitors, and doing a complicated statistical analysis, again, not perfect science, it appears that those patients who had elevated LP(a)had the highest risk of the patients in the trial and those who got a drop in their LP(a) on PCSK9 inhibitors seem to have some additional benefit beyond what would've been predicted by LDL. So, we've got some new antisense drugs that are gonna lower LP(a) about 80% and, they are in outcome trials right now and if those trials show significant benefit, then again, it'll be to the detriment of apheresis centers, but certainly to the benefit of patients.

Dr. Sorrentino:
Well, thanks, Alan for your insight into the state of prevention today. It was great to be able to discuss this with you today and see how the field is changing and continuing to grow. Thanks so much for joining us.

Dr. Brown:
Thank you very much, Matt.

Dr. Sorrentino:
I'm Dr. Matthew Sorrentino. To access this episode and others in this series, visit ReachMD.com/HeartMatters, where you can be part of the knowledge. And thanks for listening.