Management of the Patient With Triglycerides 200-499 mg/dl

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Dr. Brown:
You're listening to ReachMD and this is "Lipid Luminations," sponsored by the National Lipid Association. I am your host, Dr. Alan Brown, and my guest today is my good friend, Dr. Carl Orringer who recently joined the faculty of the cardiology division at the University of Miami Medical Center where he is an Associate Professor of Medicine and Director of Preventative Cardiovascular Medicine, as well as the LDL Apheresis Program. So today, Carl and I are going to discuss the management of patients with modest hypertriglyceridemia in the range of 200-499.

Carl, thank you very much for joining us.

Dr. Orringer:
Great to be with you Alan.

Dr. Brown:
So this is an important topic to talk about, especially in light of the current guidelines, which basically base statin treatment on level of risk and haven't focused too much on numbers. Obviously we are not here to debate that, but I want to hear a little bit more about your thoughts about what should the practicing physician do when he has a patient whose triglycerides are 350? How should he approach it? Is statin therapy going to be adequate?

Dr. Orringer:
Well you know, the problem of high triglycerides reflects, in general, problems that relate to lifestyle. In most of our patients, there are dietary issues, particularly the increased intake of saturated fats, meats that are fatty, the skin of poultry, 2% or higher dairy products, and occasional saturated fats related to processed foods. In addition, though, those patients also are consuming higher amounts of simple carbohydrates: pies, cakes, candies, cookies, fruit juices, alcohol, white flour products, white rice, white potatoes, white pasta and fast foods. And all of those are the fuel for triglyceride formation.

When triglycerides are elevated, we have 2 major concerns. When they are in the range of 500-999, we are thinking of increased risk of coronary disease, but we also know that chylomicrons are present even when triglycerides exceed 500 mg/dL. When they are greater than 1,000 mg/dL, we are in pancreatitis territory and we are very concerned about that risk as well. Now, more often though, we see patients clinically with triglycerides in the 200-499 range, and in those patients, we know

Host

Alan S. Brown, MD, FNLA
Director
Prevention Center/Lipid Clinic for Midwest Heart Specialists
PARK RIDGE, IL

Clinical Associate Professor of Medicine and Cardiology; Loyola University Stritch School of Medicine
MAYWOOD, IL

Guest

Carl Orringer, MD, FACC, FNLA
Associate Professor of Medicine, Cardiology Division, University of Miami Medical Center
NEW YORK, NY

Program Description

What are some of the causes of high triglycerides? What is the biggest health risk? And, for these patients, at what level is the risk greater for developing pancreatitis and coronary artery disease? Host Dr. Alan Brown welcomes Dr. Carl Orringer, Associate Professor of Medicine at the Cardiology Division, University of Miami Medical Center and Director of the Preventive Cardiovascular Medicine and LDL apheresis program. In this edition of Lipid Luminations, Dr. Orringer will discuss the management of the patients with triglycerides 200-499 mg/dl.

Sponsorship Acknowledgement

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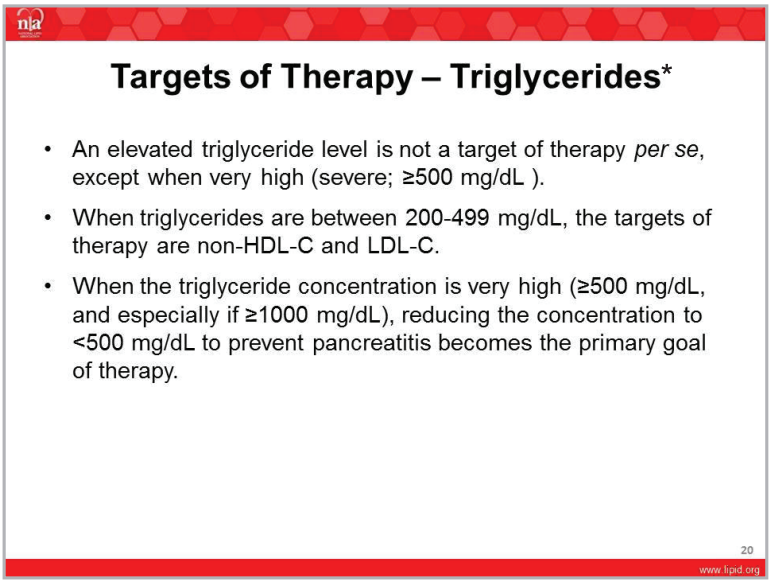
that these patients are at higher risk of atherosclerotic cardiovascular disease than those who just have high LDL cholesterols alone. So it is the combination of high LDL cholesterol and high triglycerides that places these patients at increased risk. So, we want to be vigilant about that and we want to be thinking about risk reduction strategies that will work for those patients. And in the great majority of patients, this relates to improving a patient's lifestyle.

But before we talk about what we need to do for these triglyceride levels, I want to backtrack a little bit and talk about what triglycerides are. Triglycerides are produced types of fats in the body that are used to deliver fatty acids to muscle for energy utilization and to provide storage of energy in adipose tissue in case we starve, and that is how triglycerides were basically developed by someone who is much higher than we are. But the problem is that most of us are not in a starvation state and most of us, in fact, are at an overnutrition state, and therefore the triglycerides will accumulate in fatty stores in the body, and so you see patients who are carrying excessive adipose tissue and that is frequently associated with hypertriglyceridemia. So our objective needs to be thinking about what we can do to minimize both cardiovascular risk and pancreatitis risk related to these elevated triglycerides.

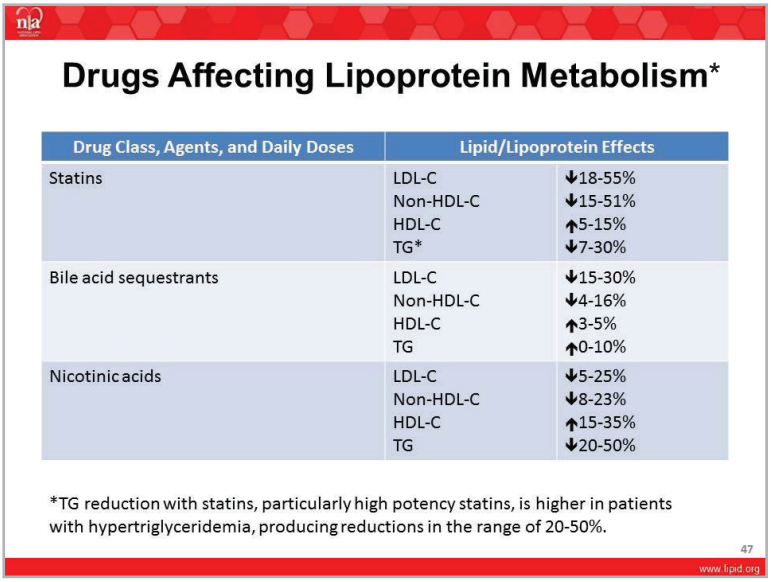
Dr. Brown:
Okay, well since our topic is focusing on the more modest elevations and where the risk of pancreatitis would be relatively low, but the risk of atherosclerosis is significantly elevated, what do you think about this strategy of obviously focusing on lifestyle and giving a moderate to high-dose statin as recommended by the AHA/ACC? How much expectation would you get to see the triglycerides come down? You know the LDL is going to come down. And how do you determine who has residual risk after you make that intervention?

Dr. Orringer:
So, what we recommend, and in concert with the National Lipid Association recommendations for the patient-centered management of dyslipidemia, our suggestion has been when a patient is found to have triglycerides of 200-499, the clinician should measure non-HDL cholesterol. Non-HDL cholesterol is a simple measurement of total cholesterol minus HDL cholesterol, and the usual goal for that is 30 mg/dL above the LDL cholesterol goal. So, what we do know is that when the non-HDL cholesterol is more than 30 mg/dL above the LDL cholesterol goal, that means that the patient still has residual risk and should be treated more aggressively. As you pointed out a minute ago, the first step that we always use is intensification of lifestyle therapies, dietary approaches and cardiovascular exercise. When we talk about cardiovascular exercise, we are talking about an initial goal of 150 minutes of cardiovascular exercise per week, ideally 5 sessions per week, ideally 30 minutes or more per week, and that is for weight maintenance. If you are talking about weight reduction, you are talking about 200-300 minutes a week of moderate or higher intensity cardiovascular exercise. Now, when people hear this, they say that is impossible, it is too much, it can't be done and the answer is that some is better than none, just like some dietary change is better than none. And when those approaches are inadequate to address the non-HDL cholesterol goals for the patient, then under those circumstances, one should consider the use of drug therapy, and statins clearly are the primary therapy for patients with triglycerides of 200-499 when lifestyle change therapy has been inadequate to lower those levels.



Dr. Brown:
So, let's talk about that for a second because I think over the years, you and I have seen physicians choose fibrates before a statin, niacin before a statin, but actually statins will bring triglycerides down significantly at appropriate dosages, right? So what can a doctor expect when he starts the statins? And I only bring this up because it is one of the critiques you hear out in practice about nobody thought about the intermediate range triglycerides and I know the NLA is addressing it in their recommendations, but what should a doctor expect if someone gets put on a moderate to high-dose statin in terms of triglyceride lowering?

Dr. Orringer:
So one can traditionally see a 35%, or even more, reduction in triglycerides, particularly in the higher dose ranges of statins, and sometimes you can have 40-45%; it depends upon the level of triglycerides. And in fact, there has been a movement to consider statin therapy in the absence of acute pancreatitis history for patients with triglycerides of 500-999 because they have been shown to have such profound triglyceride lowering effects. The other advantage, of course, and we know about all of the other beneficial things that statins do, so you get the benefits of triglyceride reduction with statins as well as the benefits on cardiovascular risks.



Dr. Brown:
Just going back to the excellent point you made earlier about non-HDL as a predictor of risk; once you have gone ahead and initiated therapy and used, if appropriate, statin therapy, and then you recheck the numbers, what percentage of people are going to have a residual high non-HDL? Do you have some rough idea? And then, that is where we get into the question of what to do next, that lipid specialists, like yourself, can help our audience with. So the first question is, what percentage of people with 200-499 triglycerides do you think will get their non-HDL under control with the recommended dosages of statins? And the second one is, for that percentage that do not, what is the next step, beyond lifestyle, which you have already… ?

Dr. Orringer:
So it is important, first of all, to recognize that with statin therapy, you traditionally see a very substantial reduction in triglyceride levels in many patients in that 200-499 range. And then when you follow them the next time, the triglycerides have gone up, and the reason that they have gone up is because, in many cases, they have continued to take their statin but they have liberalized their diet. So we always tell people that when you start a statin that is not your license to forget lifestyle. It is important to continue on your lifestyle efforts and, in fact, sometimes the more careful attention to lifestyle may reduce your need for medication if substantial triglyceride elevation is present. But in most cases, we are recommending today the initiation of moderate or high intensity statins anyway in those who require statin therapy, and those doses do have substantial triglyceride lowering properties. But it is clear that many patients do get that initial marked downward bump in triglycerides, and then when you follow them up, their triglycerides have gone up again. It is almost always due to dietary issues.

Dr. Brown:
So when that happens, obviously you refocus on lifestyle, but do you ever consider adding another agent for specifically triglyceride lowering, especially considering the results of the clinical trials and what might be the wrong patient population being studied, etc. But now I am asking for your expent opinion.

Dr. Orringer:
Okay, so now when you see that you are always asking the question, "Is there anything else that is driving this triglyceride elevation?" So the most common clinical scenario is that the patient has either overt diabetes that you didn't know about or has impaired fasting glucose. Glucose is one of the fuels for triglyceride production, so you always want to be vigilant that the patient has not kind of slipped into a diabetic state or has impaired fasting glucose. Are they hypothyroid? Do they have other metabolic abnormalities that would account for their elevated triglycerides? Are they taking various medications that can raise triglycerides? And patients who are on steroids, patients who are on HIV treatment, sometimes patients who are on thiazide diuretics, rarely patients who are on beta blockers. These are all agents that potentially can raise triglycerides. You may get referred a patient who is being treated for acne with isotretinoin. So there are a lot of options that you might want to consider. If none of those options are present and the patient's triglycerides are just getting worse, I would really ask them to give you a diet diary. Because, in fact, many patients who feel that they are doing well are actually making dietary errors; they are doing things that unintentionally are causing their triglycerides to go up, and sometimes a simple analysis of their dietary habits can make a big difference.

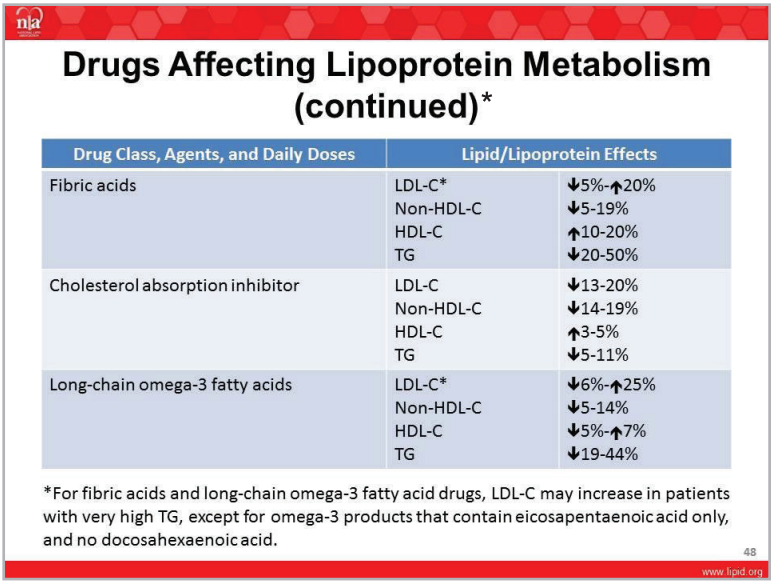
Dr. Brown:
So I think what I am hearing from you is that you make your risk assessment; you go ahead and put them on the appropriate dose of statin if they qualify, in terms of risk; you focus on lifestyle as the first step, even before the statins, and then if they still have a residual high non-HDL the first step is to just be a detective and look for what else might be going on. You have been very hesitant to mention adding any additional medicine in that patient who still has a residual high non-HDL. So I will ask you, why the hesitation? Is it wrong to be considering things like fenofibrate, niacin or omega-3 fatty acids as an addendum? And should those be reserved for people with triglycerides over 500 in your opinion?

Dr. Orringer:
Now we are into a gray zone. It is not that the drugs that you suggested do not lower triglycerides, the question is do they benefit the patient? I first want to talk for a minute about the omega-3 fatty acids. We always advocate increased fish consumption for those who have elevated triglycerides, certainly 8 ounces or more of ocean fish per week makes a lot of sense since that has been associated with lower cardiovascular risk. We don't know if that applies to people who are taking statins, however, because that was data that came in the pre-statin era. Nevertheless, people who are eating more fish are eating less saturated fats, so it is a good dietary habit to get into. The question becomes should omega-3 fatty acid supplements be recommended in those patients, and if so, should you consider non-prescription omega-3 fatty acids, or should you consider prescription omega-3 fatty acids? Well the first thing is, is that the FDA has not as yet approved the use of prescription omega-3 fatty acids for patients with triglycerides that are less than 500 mg/dL. So, the use of these agents by the clinician is a clinical decision that is made based upon a clinician's preference. It is just not evidence-based at this point.

Dr. Brown:
Yes, and so, the reason the FDA has not given them an indication in those patients is the data for its benefit in reducing cardiovascular events is not strong enough.

Dr. Orringer:
That is correct. We actually find that in surveys that we have done, and we actually just completed a triglyceride survey of almost 500 individuals, many of whom were National Lipid Association members, we find that there still is a significant prevalence of use of omega-3 fatty acids even in that group. So again, the clinician has to decide what he or she thinks is appropriate, but the evidence base at this point is not there to support its use in prevention of cardiovascular disease in the 200-499 range.

Then there is the issue of whether fibrates should be added. The studies that have looked at fibrate therapy on top of statin therapy have shown that clearly triglycerides can be significantly lowered, but there have been no demonstrated benefits in terms of atherosclerotic cardiovascular disease risk prevention in those studies that have been done. So, again, it is a clinical decision. It can make the numbers look better, but whether it makes the patient better is another question.



Niacin therapy does everything that you could want in terms of lipid improvement, based upon its ability to lower triglycerides, raise HDL cholesterol and in high enough doses, lower LDL cholesterol. Whether niacin therapy benefits patients in the 200-499 range remains to be seen. Niacin therapy has fallen out of favor a good bit recently based upon the results of AIM-HIGH and HPS2-THRIVE, but those were in very specific populations of patients who were already statin treated and intensively statin treated. Whether niacin therapy is useful in those patients who have modest triglyceride elevations when diet and exercise has been inadequate to treat them, remains to be determined. So again, it becomes an issue of clinician preference.

Dr. Brown:
Great. Well I can't thank you enough for your insights on hypertriglyceridemia. I think it will make a lot of people comfortable that it is not as complicated as we think, but not easy because the focus on lifestyle is so critical.

Thank you very much Carl, as always, for joining us.

I am your host, Dr. Alan Brown, and you have been listening to "Lipid Luminations" sponsored by the National Lipid Association on ReachMD. If you have missed any part of this discussion, please visit us at ReachMD.com/lipids to download this podcast and others in the series. Thank you very much for listening and thank you, Carl.

*Jacobson, Terry A. et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: Part 1 – executive summary. Journal of Clinical Lipidology. Volume 8 , Issue 5 , 473 – 488.

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