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Dyslipidemia During Pregnancy: The Risks for Two Patients

Doctor Alan Brown:
You are listening to ReachMD, and this is Lipid Luminations, sponsored by the National Lipid Association. I'm your host, Doctor Alan Brown, and with me today is my good friend, Doctor Robert Wild, who is the Professor of Reproductive Medicine and Director of Research and Development in the Departments of Obstetrics and Gynecology as well as Family Preventative Medicine including Biostatistics and Clinical Epidemiology at the University of Oklahoma. He's also the Chief of the Gynecologic Service at the VA Medical Center in Oklahoma City.

So today, we're going to talk to Bob about dyslipidemia and pregnancy. It's an issue that many of us in lipid clinics get consultations regarding. I think a source of a lot of confusion for many of us so I'm thrilled that you took the time out of our meeting to talk to us today, Bob.

Doctor Robert Wild:
Well, good morning. Thank you for having us.

Doctor Alan Brown:
In my earlier years of training, there used to be a saying, "Never draw a lipid profile on a pregnant female because it'll just make you crazy." With that said, why the heck do we even want to know what the lipids show in pregnant mothers?

Doctor Robert Wild:
I think your illustration of training and the differences as to why is kind of right on. We used to think that what happened to the mother doesn't affect the baby, doesn't really have long-term implications because it's only nine months, and we now know that's definitely not true. We know that keeping the mother under control has dramatic impact on how the fetus will do, how her obstetrical outcomes will be improved and what impact is important in terms of her long-term risk because of the stress of pregnancy, because of the fetal programming that's affected by what happens to the mother and how that child will be launched into that child's childhood, and ultimately, we can track challenges for that child's long-term outcome.

Doctor Alan Brown:
So that's very interesting, that nine months of dyslipidemia has an impact on the adulthood of the fetus?

Doctor Robert Wild:
We used to just think it was a blind spot, like why do we need to mess with this? It's a short deal, but we now have lots of indicators that we can predict if the mother has a problem, that means more problems for her later in life, and if the mother isn't in control, that means that the child has fatty streaks to develop, and that can be traced even in childhood where, if the child's lipids are normal, but the mother was out of control, there's still fatty streaks.

Doctor Alan Brown:
So Bob, this opens up a bag of worms. I'm very interested in this. Who do we have to worry about in terms of the pregnant mother? Should we be routinely ordering lipid profiles during pregnancy or are there particular individuals that we're going to want to follow during their pregnancy?

Doctor Robert Wild:
I advocate, and I think we have enough information now to suggest it's going to be quite worthwhile that we screen virtually everybody as part of a standard evaluation for two reasons. One is we can screen for ____ (2.41) when others have not. Another reason is we can see when patients are out of control. We can pick up genetic disorders. That doesn't mean we have to hit them with a heavy hammer. It

means we can intervene in terms of quality nutrition that has an impact on that mother and her weight changes for that mother and her long-term risks, potentially her obstetrical complications and with indirect effects on the child.

Doctor Alan Brown:
So let's drill down that a little bit. Does every mother who is pregnant develop some sort of dyslipidemia, and when do you get worried, assuming we're going to draw lipid profiles during pregnancy? So my questions would be when should you draw them, in what stage of pregnancy? What should you expect and consider it normal, and then in whom would you get concerned?

Doctor Robert Wild:
I would say as a matter of routine panels, if it hasn't been done by our current recommendations, either pediatric or ____ (3.33) recommended, all people should know where they stand, and if it's normal, I think you're good unless there's a potential complication or a problem. If there's a problem, that's a whole different ball of wax, and we should begin to act on it. Some would recommend that perhaps every trimester, it's worthwhile. I think we need to further understand whether that's cost effective or not. What are normal values? We used to not know that. Now, we have data over 9000 plus persons to point out that the average cholesterol or triglycerides usually doesn't get above 240, 250 milligrams per deciliter, and it's very interesting. That data is in normal people, older data from the late 70s shows that the values are slightly higher, like around 300. Why is that? That's because that includes people with complications, and we know that if we include people with toxemia in pregnancy, gestational diabetes, those triglyceride values can get around 300 on an average, and it you're talking about an average, that means they can go much higher than that. So anytime it gets to be about 250 or so, we should be concerned.

We also know that if we screen in the first trimester, there's a linear relationship between triglyceride elevation and risk for toxemia in pregnancy and gestational diabetes. If we understand what happens to the mother during the pregnancy, pregnancy state of insulin resistance so lipids will rise on the average to be most excessive in the last trimester. That goes for both cholesterol and triglycerides, and then we can show postpartum when they come down, and if they've had a complication, they don't come down the way we want to, and we want to be comfortable that those people are not lost. They're evaluated and treated for their condition because they've just endured a stress test.

Doctor Alan Brown:
If you see somebody whose triglycerides are 350 versus someone whose triglycerides are 1000 at the end of the first trimester, what would be your approach to those two types of patients?

Doctor Robert Wild:
Somebody with a triglyceride around 350 is too high, and she may well be at that level because of dietary indiscretion. She may be at that level because she's developing early signs of toxemia or she's a diabetic or pre-diabetic or she's just being uncovered as a diabetic. The more common reason for a high elevation is gestational diabetes. So of course, knowing what happens prior to pregnancy is important in interpreting how you evaluate the given value in pregnancy. When you get triglycerides that high, you got to begin to wonder, is it through a genetic reason for that or propensity to it from dyslipidemia point of view. Once you're comfortable that it's not diabetes related, you got to be able to treat it just by virtue of its level. So she may well be at risk for gestational issues or she may have either primary or secondary causes for that triglyceride. What are reasons and things to think about? Well, the usual things we rule out, alcohol use, drugs, medications that are widely used or misused, potentially a genetic disorder. We got to rule in and out those things we would do whether or not she's pregnant, but keep in mind that within our differential, we got to think about ___ (6.40) complications.

Doctor Alan Brown:
If you're just tuning in, you're listening to Lipid Luminations on Reach MD. I'm your host, Alan Brown, and I'm speaking with Doctor Robert Wild about dyslipidemia in pregnancy.

Now we get down to the 350. I assume you would focus on treating the underlying cause, trying to put the patient on a good diet, maybe some weight loss or it might be appropriate during a pregnancy, but then you have the dilemma of the one who's 450, 500, 1000 where medication or some other intervention would be required, and we all get nervous about giving almost anything during pregnancy. What are the lifestyle changes that are safe during pregnancy? Is it safe to put someone who's pregnant on a calorie-restricted diet? Then secondly, if you do have to use medication, what's your threshold for using the medicine, and what do you choose?

Doctor Robert Wild:
It is safe to keep people on calorie restrictions, and if you go to the Institute of Medicine, you can look up recommended weight goals per trimester and try to keep people within those goals for whatever it takes. If it's first trimester, second or third trimester, you can keep people within norms. We use to, on the average, think about 28 pounds, what does that mean? Well in somebody that's really heavy to begin with, you don't need to be that high. If somebody is average you can keep them more average, and if somebody is on the other side, you can adjust accordingly. So you keep the calories in conjunction with the diet and exercise recommendations just to keep them

with what we would know normally in a non-pregnant person. Basically, eating heart healthy is wise in pregnancy just as it is pre-pregnancy.

Doctor Alan Brown:
Now, that's interesting. When you look at family history, and everybody points to genetics. Some of the family history is what you eat in the household.

Doctor Robert Wild:
That's exactly right.

Doctor Alan Brown:
That whole epigenetics discussion that you had earlier about effect on the fetus starts when they get home too, I suspect. So let me get back to the question of triglycerides are 3000 now, and there's first trimester, under their first trimester, and you're nervous. I would be nervous. You're worried a little bit about the development of pancreatitis. How nervous should I be, and then what are safe treatment options beyond lifestyle modification?

Doctor Robert Wild:
You should be nervous because if you've ever taken care of somebody with pancreatitis in pregnancy, it's a real mess and challenge. I mean, it's really difficult to deal with. We talked a little bit earlier. There are some people with a genetic propensity to have high triglycerides, and they're not going to get pancreatitis. Unfortunately, it's tough to genetically test for that or understand that, and there's a significant number that are. People really get concerned if they're symptomatic in any way, and think about what pancreatitis causes in a non-pregnant person. Well, the same thing is going to happen. You still have to look for eruptions on the skin. You still have to look for abdominal mid-epigastric discomfort. You still have to think about those things you would in a non-pregnant person. Yeah, it is important. If they're symptomatic, they definitely need to be treated, and if they're really sick, they need to be hospitalized. If they're hospitalized, the first rule is to find out if their diabetic because you have to treat that in addition and keep people under control. People need to be brought in, become NPO. Sometimes IV insulin is needed to keep people under control. Sometimes if they're not diabetic, just keep them dehydrated, the help of a nutritionist that can do parental energy supplement is a goldmine if you have it. Those people are absolutely wonderful.

So in the acute phase, there are anecdotes of lots of different ways to treat it. We don't have any systemic solid information to say that's the best way. I think what we do is we go with the safest way we know. Keep somebody NPO. Keep their fat content down. Some experts would say 10 percent or less or 15 percent, I mean way down. We know that we can definitely have an impact. _____ (10.25) nutrition is probably the best way to go. There are some people that ultimately, you don't have that or you have other ways to treat them, and some people respond to plasmapheresis with all of its challenges. Those could be dealt in an acute situation, but they do go home. So after you've dealt with them, how do you take care of them afterwards? Turns out that widely used in different parts of the country are different treatment strategies. Historically, gemfibrozil's been used. Gemfibrozil is a class C drug widely. Particularly in early trimester, fish oil is used, and it's used with the thought that maybe there's no risk. It turns out fish oil is a class C as well.

What does class C mean? Class C means that if you need to use it, you've got to use it, and if you have alternatives, you got to use the best alternatives. We're talking about triglycerides disorders, but it's useful for all of our audience to be able to understand that you can look up the class of medication. There's often an alternative. We're talking about triglycerides, but what if it's an LDL problem? By all assets, ____ (11.30) that are easily used. They're class B. Mipomersen is a class B drug for the right person if you can get a person on it. The other agents are class C, but that means you don't necessarily not use them if you have to use them.

Doctor Alan Brown:
So we just have a couple of minutes left. I would like to ask you for the asymptomatic patient with a triglyceride of 3000. Are you using anything or are you focusing on diet?

Doctor Robert Wild:
Mostly, it's diet and nutrition. If we feel uncomfortable, widely used is fish oil without data and with concern, but you can get amazing drops in triglycerides just by getting people off of refined sugars and dietary intervention in keeping fat down. It's really pretty amazing.

Doctor Alan Brown:
Let's go back to the ___ (12.11) you mentioned earlier which is an important part. We'll leave the topic of triglycerides, and I assume when you were talking about using a ____ (12.18) or mipomersen, you're talking about people with severe LDL elevation and normal triglycerides.

Doctor Robert Wild:
Right.

Doctor Alan Brown:
Once you diagnose ____ (12.27) because you did your routine pregnancy screening, at least it gives the opportunity to capture these patients, and then you'll screen the baby and maybe do a great service for them.

Doctor Robert Wild:
... and the family.

Doctor Alan Brown:
So in a young female who's pregnant, is there the same sort of epigenetic problem going forward? You know, traditionally, my approach to ____ (12.45) in pregnancy is stop the medications a month or so before they try to conceive, and I hold off on medications until after they're done lactating, and at that point, I put them back on the ___ (12.57) because of my thought that at that relatively young age, being off ____ (13.00) for eight or twelve months is probably not that bad a situation. Am I wrong about that?

Doctor Robert Wild:
Well the ____ (13.08) recommends get off ____ (13.09) because it's a category X. Of course, the data behind that, you have to realize that even in the third trimester, there are case reports of people using ____ (13.17), and the thing to remember for us as lipidologists, the predominant congenital ___ (13.21) risk is in the first trimester. So we have more leeway and more options available in the later trimesters because of the way the process works.

Now LDL that's high, we really shouldn't ignore. As far as we can determine, the ____ (13.35) risk is better described and certainly in animal models and in some of the studies we have for childhood atherosclerosis, better understood for out of control LDL than it is for triglycerides.

Doctor Alan Brown:
So in our guidelines for ____ (13.50), it tells you basically stop the therapy until after they're done breastfeeding, but in your practice, do you switch over to a ____ (13.57) during a pregnancy?

Doctor Robert Wild:
Yes, we have good inkling and good information that the lower the LDL, the better and it's always a risk benefit of what cause, what expense, how difficult to pull it off. There's always the challenge that somebody with ___ (14.10) when somebody says, "Well, you can't get pregnant." Well, often my patients say, "Forget that, I'm going to do what I want to do," and we need to be equipped to be able to handle it.

Doctor Alan Brown:
Now, that's terrific, Bob. I can't thank you enough for your insights in dealing with this confusing issue to most of us. You obviously have clarified a lot of issues, so thank you for being with us today. Unfortunately, we've run out of time. I could spend the afternoon talking to you.

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