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Selecting the Right Contraception for the Dyslipidemic Woman

Dr. 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 my good friend, Dr. Robert Wild, who is the Vice-Chair of the Department of OB/GYN and Adjunct Professor of Family and Preventative Medicine, as well as the Chief of Gynecology at the VA Medical Center in Oklahoma City. Bob is also a member of the Board of Directors of the National Lipid Association and an ultimate lipidologist. He's one of our great resources because you have this expertise in both OB/GYN, pregnancy, and dyslipidemia, which a lot of us cardiology geeks and internal medicine geeks don't have. So I'm really excited to talk to you today about choosing the right contraception in women with dyslipidemia. In fact, I'm particularly excited because I've had questions on this before and I never hesitate to call you and ask for your advice.

Dr. Wild:

That's a great part about the NLA, just pick up the phone and talk to somebody, share ideas. It's wonderful.

Dr. Brown:

Yes. Well, you definitely helped me in a patient that I had with hypertriglyceridemia, so I'm going to…

Dr. Wild:

Two-way, two-way street.

Dr. Brown:

You can share me with some of that. So, and I probably didn't mention that you're Adjunct Professor of Family and Preventative Medicine and the Vice-Chair of OB/GYN is at University of Oklahoma.

Dr. Wild:

Yes, it's at OU.

Dr. Brown:

Right. And the Chief of Gynecology is at the VA Medical Center, right?

Dr. Wild:

Right. In Oklahoma City.

Dr. Brown:

Okay. I want to get your credentials right. So Bob, let's talk about this a little bit. This is a real common problem in terms of being fooled sometimes where you have a young lady with severe dyslipidemia, they get labeled as FH, and it turns out it's possibly their contraception they're taking, or even though it isn't directly our topic, drawing blood work on pregnant women and trying to interpret what the heck to do with it. So, let's talk a little bit about types of dyslipidemia you might see in a woman of childbearing age, first of all, and who also wants to be on contraception, and how would you make a choice? That would be the first question. And then the second question is, if you get a patient referred to you who's already on contraception and you see dyslipidemia, how do you sort out whether the contraceptive is the culprit or the patient has some underlying lipid disorder?

Dr. Wild:

Okay, both are good questions. Let's go to the first one. I think the way to think about it is just like we tend to think of dyslipidemia. Think about challenges with mixed dyslipidemia or LDL disorders, in this case familial hyperlipidemia. So, why do we screen reproductive-aged woman? Because we want to pick up early those conditions we can make a large impact. So, when we screen, we screen for FH, either homozygous or heterozygous, we look for mixed dyslipidemia, which are common with an ever-increasing obesity concept. The problem is, is we could have another enzyme defect in addition when we measure a lipid profile and screen properly. So, screening is important. Now, when we start to counsel people regarding contraceptive choices, it's important to make an accurate diagnosis, understand targets and goals, and understand how contraceptive choice impacts that. So, what do we do? Let's say we have a patient who, in spite of appropriate diet and exercise, has other concerns to help drive a contraceptive choice. The thing to remember for all of us is, is the risk to her if she becomes pregnant, is riskier than any contraceptive choice we make. So, we've got to weigh risk and benefit balance choices to make an appropriate decision.

Dr. Brown:

So, in that case you're talking about someone maybe with pretty significant hypertriglyceridemia where getting pregnant might aggravate that and be a serious health hazard to her.

Dr. Wild:

Correct, or if she has FH, regardless, or if she has an unusual factor V Leiden problem. The real choice for considering contraceptive choice is, I think, number 1, what's going to be making her adherent and, I think, understanding thrombotic risk. So, we have to take that into consideration as well as the changes that will happen to the lipids when the patient's on a given

contraceptive choice. So, what do we do? Well, we assess her cardiovascular risk profile, like we would anybody else, and then we try to decide for her what's going to work for her. So, how do we think about that? Well, if she's young she has theoretically less risk, whatever the disorder. If she gets older or has another comorbidity, let's say obesity, then her thrombotic risk goes up. If she has a family history that is positive for clotting problem or lipid problem with associated atherogenic vascular change, then her compounded risk goes up. If she has, let's say, factor V Leiden, she's got a risk with the pill, but if she has factor V Leiden and then she gets pregnant, that risk is many times as high. So, it's a contraceptive choice, understanding that doing nothing and letting her get pregnant is riskier than whatever choice she makes. So, if she is young enough, there are a lot of considerations that go into a choice for her. She has to understand menstrual function and how it works; she has to understand the side effects with whatever treatment option we give her; she's got to understand what is she going to use that's going to make her compliant, what's her situation? Is she sexually active at risk now? Is she going to plan to be later? That's all important. So, how to make a choice. Well, we try to explain what we can for, in terms that patients can understand, what the risks and benefits are with every single choice. So, it does make a difference if she has a high LDL or high triglycerides. We know that if somebody has significant hypertriglyceridemia, uncontrolled, for either an enzyme, polygenic or **monogenic*6:06** reason, enzymatic reason, that is not a good situation where we use combination oral contraceptives if they have an estrogenic component. That'll definitely aggravate their triglycerides and we could actually precipitate a pancreatitis. It turns out that if she takes transdermal oral contraception or vaginal contraception, we don't get any wiggle room. There's the same kind of risk as it is with combination pills. So, what does that leave us with? Well, she may want to use an implantable Implanon progestin-only medicine. In general, those tend to be fairly lipid neutral. She may be challenged with weight gain concerns incidental to either of these two disorders, or part and parcel with part of them, and then, I don't like in certainly a young reproductive-aged woman who may want to have fertility in the future, giving somebody like that Depo-Provera which is an injectable progestin. The reason is, so many of them have weight gain problems and then they aggravate their insulin resistance. So, probably one of the better choices is an IUD, and there are several on the market and several coming on the market. There is a progestin-only, the more widely used one now is the Mirena, which is a 5-year progestin-only, very active in the uterine cavity, sometimes associated with irregular bleeding in the beginning, but then over, after the first 3 months, commonly associated with lack of menses altogether. There's Skyla which is now a 3-year similar type device to the Mirena, but it is 3 years' less medication. It's important to realize with both medicines, they're circulating progestin and that progestin is slightly androgenic. With a higher dose you can have slightly greater impact on lipids and you could use a progestin-only pill. The challenge with a progestin-only pill is you've got to remember to take it, hopefully at the same time every single day, so you have to have a compliant person, and you've got to realize that oftentimes vaginal spotting leads to a lack of compliance. So, those are all important considerations in terms of choice. Now, how do we classify and how do remember what's a good choice and how can we pay attention to all of this? Probably the best thing to tell people is there are two great websites to go to to help people understand appropriate choices with multiple medical comorbidities to make choice. Let's say we're focusing on dyslipidemia. You can go to the CDC, go under medical complications, there's a wonderful chart in there that'll give you a classification of risks and benefits for each type of contraceptive choice. And if you look very carefully, let's say for example, combination oral contraceptives, or let's say a Mirena, which is the progestin-only, they'll be classified. You might see, you'll note that all of them are Class 2 which means use when the benefit seems to outweigh the risk, but there are maybe 2 or, Class 2 or 3 for the combination oral contraceptive and the transdermal preparation or the vaginal preparation. So, that weighs in your decision. I think the overall thing is an informed patient understanding how she's going to be compliant and use it and what works for her. And it really depends a bit on her situation. She's a young gal that wants to go off to college and she's not sexually active now but she never knows when she's going to be and we're dealing with this dyslipidemia, the nice part about not having to remember to take a pill every day, and the progestin IUD has a real benefit for compliance and maintaining something that's useful. The major risk is with insertion and that risk is really quite manageable. Most people do well if they've never been pregnant or if they've had multiple pregnancies. Sometimes there are other gynecologic conditions that now have to make us make an appropriate other choice and we need to pay attention to that. Later, in reproductive years, above age 30, roughly 30% of women have fibroids and that can distort the uterine cavity. It's a relative challenge for an IUD. So, we've got to make a couple of choices when we have certain complex, or more confounding gynecologic conditions, in addition to our concern about dyslipidemia.

Dr. Brown:

So, that's really a fantastic review. I didn't have to interrupt you because you reviewed everything. But, I wanted to ask you, if I'm getting you right? So, you try to avoid the estrogen component with hypertriglyceridemia.

Dr. Wild:

You really do because you can precipitate a pancreatitis with an estrogen-containing combination pill.

Dr. Brown:

Sure. Same thing we think about in postmenopausal women in terms of how much estrogen we're going to give them, but one thing we talk about in the postmenopausal woman with hypertriglyceridemia, which I thought was intriguing about what you said, was that we'd switch them to transdermal and it seems like they don't get the same triglyceride elevation, but you mentioned that transdermal combination contraceptives still affect the triglycerides?

Dr. Wild:

They really do and so does vaginal…

Dr. Brown:

Am I wrong in assuming that estrogen replacement therapy in a postmenopausal woman is better given transdermally if they have hypertriglyceridemia?

Dr. Wild:

We tend to think that the transdermal approach to estrogen-only has less of a first-pass oral effect, so the triglyceride-raising challenge is not as severe. Don't forget though, there can be a second and third pass to the liver. So, it will help by making it transdermal, so it's a relative judgment issue. Now, the difference between a patch used for combination oral contraceptive in a younger reproductive-aged woman or a postmenopausal woman, is you have a higher steroid load with a combination pill. So, if you have an estrogen combination with a progestin, the way to think about that, that could be anywhere between 2 and 7 to 9 times as much steroid load compared to postmenopausal estrogen. So, now you've got a larger steroid load and it turns out the thrombotic risk seems to tract the same, whether it be transdermal or vaginal or combination oral contraceptive. So, it's thrombotic risk that drives our decision-making and then we watch the reflection on the lipids and it's important to realize that when people are taking these preparations, there are changes in lipids. Now, the good news is, on the average, those changes are not dramatic as we would call dramatic, like 50% LDL change or whatever, but they are quite noticeable depending on the type. So, we've got to understand how that works. And it turns out, and I don't want to make it too complicated, but the type of oral contraceptive has an effect depending on what's in it. It's hard to…it's the kind of thing you need look up on a chart, but the way to think about it is the more total estrogenic effect, the more triglyceride raising, and that could be as high as 20-30%. The more estrogenic in the overall content of the pill, the better the LDL lowering and that's not dramatic, but it's noticeable. And the HDL raising and pills convert into progestins or androgenic progestins it's really more complicated than that. It's an estrogenic, anti-estrogenic, progestational,

androgenic, antiandrogenic combination. Well, sum total is, basically, what's the effect? What's the bioassay effect? The bioassay effect seems to be such that the more estrogenic overall effect, the lower the LDL on its use complicated by how long it's used and other comorbidities that intervene. In general, the more estrogenic, the higher the triglyceride raising. If you use a progestin-only oral contraceptive or injectable or Implanon like an injectable progestin, those tend to be a little more lipid neutral because of their predominantly progestational effect. On the other hand, you don't get off scot free because you've still got to monitor them.

Dr. Brown:

So, if you're just tuning in, you're listening to ReachMD and I'm Dr. Alan Brown. With me today is Dr. Robert Wild, Professor of Obstetrics and Gynecology and also an Adjunct Professor of Family and Preventative Medicine at the University of Oklahoma, and Chief of Gynecology at the VA Medical Center in Oklahoma City. So, Bob, that was a lot of stuff. That was very interesting. I, at least, have this feeling -- I hate to quote my experience, that I've had a couple of cases that I thought had FH actually with quite LDLs in young women who are on contraceptives and I stopped their contraceptive just to see what would happen and not all of them, but at least several of them, had their numbers improve. So, we tend to think that the triglycerides are going to be affected by oral contraceptives, but how common is it to see the LDL high, and when would you suspect when you have such a patient that it might be their contraceptive versus a genetic disorder like familial hypercholesterolemia?

Dr. Wild:

Well, the first thing I would do is look at the type of contraceptive they're on. In general, if it metabolizes as more androgenic progestin they're more likely to have an LDL-raising effect. So, it depends a little bit on what they're on. It also depends a little bit on what other things are going on, other comorbidities, and their diet and exercise, and what other medicines, and what environment are they in? Are they a track-star person, they haven't told you about their anabolic steroids and there are a host of things. We have to think in a contraceptive user about all the other secondary causes as well. If you want to know pure effect, the more androgenic the progestin in the pill, the more likely they're going go get -- that's in an oral contraceptive -- the more likely they're going to get LDL elevation. Now, the problem with all the studies is they're tough to compare side-to-side. There are different durations of followup: 3 months, 6 months, 12 months. So, if, like I've done, if you combine the magnitude effect they're not all head-to-head comparisons. So, they're very difficult, you can just getgeneral trends and then you can get average changes that you see in a group, but your patient may be an individual and that individual response could be quite sporadic, so it's important to know they can affect lipids, kind of predict them, look for other things, and you may run into the experience you ran into.

Dr. Brown:

Yes and I've found myself in that conundrum where I actually have to know, does this patient have FH, what's the downside if they get pregnant, because if I tell them to go off the contraception so that we can see whether they have a genetic disorder, rather than start a statin in somebody where the lipids might be due to their contraception and not due to a genetic disorder, and I always ask the patient, "What will happen if you get pregnant?" if it's a young unmarried lady who it's going to ruin her life, then we've got to weigh the pluses and minuses.

Dr. Wild:

So, you bring up an important point. It's important to think about treating her FH and assuring that her targets are directed correctly and her goals are met, and I think the NLA does an excellent job in our Special Population document for that.

Dr. Brown:

That's a good plug. Part 2 of NLA recommendations that were just published really has a phenomenal section on all special populations, but particularly, on women of childbearing age, pregnancy.

Dr. Wild:

So, it's really important to keep her FH under control, and then, in addition, assure that she's going to get proper contraceptive use that's a good quality type, so she doesn't get pregnant. She needs to know that we really don't want her to be taking a statin if she gets pregnant, but nowadays people tend to listen and learn and sometimes they have planned and sometimes unplanned. Unfortunately, across all of our populations, 50% of pregnancies, or 40% or so are unplanned. So, it depends on the setting you're in and the group of patients you're seeing, but if we can get the message across, always assure a type of contraception. There's no reason not to use statins in reproductive-age women. I think our concern and fear about "Category X" is kind of blinded us for not treating dyslipidemic patients properly earlier in their reproductive life.

Dr. Brown:

And just make sure that you tell them, I always document in the chart, somewhere between 6 and 8 weeks prior to attempting to conceive you stop your medicine.

Dr. Wild:

That's interesting. We've done a metaanalysis we've just submitted to the*Journal of Clinical Lipidology* looking at what science says about stopping it 3 months ahead of time or a month. The answer is there's not much science at all. It tends to empirically evolve. And we learned several things, that kind of reinforce what I'm saying, is when statins are needed, if you assure contraception, they need to be used. We know we have great evidence regarding it. What we learned from the metaanalysis is several things. In spite of multiple study designs, there's not really good quality evidence that, other than in animals, that the statin itself is causing the anomaly. Now, there are mixed reports and you're never going to get an appropriate randomized trial so you're always dealing with observational information with all its warts. Do a case-controlled study, you're going to find out, what's going to happen is people are going to over-report if they have an anomaly about that medicine. So, there are shortcomings, there are individual case reports, there are cohort studies, and so we've grouped them accordingly, trying to take those to study design weaknesses and here's some things we learned from that. What we learned is no good quality evidence that it raises risk for birth defects, much safer to say that in water-soluble statins versus lipid-soluble ones. No good evidence to suggest that we have to stop it 3 months ahead of time or 4 months, but if you think about it, if a person is planning a pregnancy, a lot of gynecologists will tell them, and from a family planning point of view, or a fertility point of view, it might be smart to kind of wait a cycle anyway, to be sure you're going to have a return of ovulation, and that kind of covers you in both those clinical decisions, if that makes sense.

Dr. Brown:

So stop it when you stop your contraception basically.

Dr. Wild:

Stop it when you stop your contraceptive. Wait for a cycle before you're attempting, because then you're comfortable that they're off the medicine. Now, it might surprise a lot of listeners to realize that there is now an NICHD study showing that statins are used to prevent preeclampsia during pregnancy. That's actually now published as a pilot study. It's a water-soluble one. It's a great review to look at the congenital anomaly risk with water-soluble statins.

Dr. Brown:

And your paper, looking at this metaanalysis, that's going to be in the *Journal of Clinical Lipidology*?

Dr. Wild:

We hope so. We just submitted it.

Dr. Brown:

All right.

Dr. Wild:

D. Corales*21:18 is the first author.

Dr. Brown:

I wish you the best of luck on it. I have a lot of further questions. It's unfortunate we ran out of time. I know you have some interesting thoughts on the dangers of not treating FH females during their pregnancy and what that might do to affect the fetus and the mother longterm, theoretical but fascinating. I'd love to hear more about that but we're going to have to save that for another podcast.

Dr. Wild:

Maybe we can do that on another chapter.

Dr. Brown:

Yes, absolutely. I can't thank you enough, Bob. Dr. Robert Wild, a good friend, brilliant guy, and who has an advantage point that many of us don't in terms of dealing with women of childbearing age with dyslipidemia. Thank you very much, Bob, for being here.

Dr. Wild:

My pleasure. I appreciate your invite.

Dr. Brown:

I'm Dr. Alan Brown. You've been listening to Lipid Luminations, sponsored by the National Lipid Association on ReachMD. Please visit ReachMD.com/lipids where you can listen to this podcast and others in the series. Please make sure you leave some comments and share your comments with us. We definitely welcome your feedback. I can't thank you enough for taking the time to listen to Lipid Luminations and, once again, I'm your host, Dr. Alan Brown. Thanks for listening.