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## New Perspectives on the Impact of Omega 3 Supplements on Breast Cancer Risk

Announcer: You're listening to a special Focus on Breast Cancer from Advances in Women's Health, sponsored by Lilly.

Dr Birnholz:

Coming to you from the 42nd Annual San Antonio Breast Cancer Symposium, this is ReachMD and I'm Dr. Matt Birnholz. Joining me today is Dr. Lauren Nye, Assistant Professor of Breast Medical Oncology at the University of Kansas Cancer Center. Dr. Nye is Lead Author of a feasibility study of moderate dose omega-3 fatty acid supplementation in premenopausal women at high risk for breast cancer considering future pregnancy. Dr. Nye, welcome to you.

Dr. Nye: Thank you. Thank you for inviting me.

Dr. Birnholz:

Yeah, it's great to have you on the program. So, why don't we get some background on the setting here because obviously I just made a loaded statement on behalf of your study. A lot of factors there. And as your study prefaced, there doesn't seem to be a lot known about the breast microenvironment during pregnancy and whether this plays into future breast cancer risk. So, what can you tell us about that?

Dr. Nye:

So there's some information out there that if a woman delivers her first child before the age of 30, that may be protective. And there's several thoughts behind that that our breasts go through a terminal differentiation with delivery of a child so that they can produce milk to feed the child and that may be protective. There's a big drop in estrogen levels after pregnancy that may be protective and some thoughts that we may lose some of those estrogen receptors on some of our breast cells after pregnancy that may also help reduce the risk of breast cancer. There's other studies that worry that the act of pregnancy and having a child may have a short-term increased risk associated with it. Although in the grand scheme, it seems to be an overall benefit in terms of having your first child at an early age. And when I'm interested in risk reduction in women that are at high risk for breast cancer, I'm really interested in taking on that act of risk reduction with pregnancy and enhancing it. What can we do during that time period in a woman's life to really enhance that risk reduction. And we're seeing more and more women have their first child at a much later age, so most women aren't having their first child before the age of 30, especially in medicine, but in all walks of life, and so what can we do to still assist in helping lower that risk of breast cancer?

Dr. Birnholz: And you bring up this great point about chemo prevention agents and the limitations around their use during pregnancy.

Obviously, in that period, it's a very sensitive time. Very few agents that can be used with the intent to try to prevent or diminish breast cancer risk. What can you tell us about those limitations and perhaps that's what led you towards omega-3 fatty acid supplementation?

Dr. Nye:

So, for premenopausal women, the only chemo prevention agents which are just medications or drugs that we use to reduce the risk of breast cancer in women, the only available agent in premenopausal women is tamoxifen. And we've seen some exciting data at San Antonio this year on babyTam or low-dose tamoxifen which hopefully will have fewer side effects for women, but in all of these studies, women had to be at least 35 years old and they had to not be planning to conceive because these medications can cause harm to a fetus, and so, those drugs are just not an option for young women who are at high risk and interested in chemo prevention.

Dr. Birnholz: So, then let me ask you Dr. Nye why omega-3s?

Dr. Nye:

So, there's a lot of interest in omega-3 right now as a nutritional supplement in pregnancy. It's been shown to have favorable effects for both mother and baby and then at the University of Kansas Cancer Center in our high-risk program we've previously looked at omega-3 supplementation in premenopausal women. Again, prior studies in those women over 35, not planning pregnancy, but we did see favorable changes in the breast tissue. And then when thinking about young women planning to get pregnant, estrogen may enhance the absorption of omega-3 fatty acids in the breast tissue, and so we may increase the uptake of it in the breast tissue during high hormonal states like pregnancy. And so, the thought is will that supplementation really be more effective in even younger women who are planning pregnancy? And that's my ultimate goal is to look at that. But proof, first we had to prove that young women would be interested in willing to participate in a clinical trial that involved a minimally invasive procedure, time when they may have little kids at home and be working, and they were very interested.

Dr. Birnholz:

And to swing back around on omega-3's possible protective mechanism of action, much of which still has to be elucidated, are there any effects that are purported from omega-3s on hormonal fluctuations during pregnancy? And if so, do we know how that might be?

Dr. Nye: In mice.

Dr. Birnholz: (laughter)

Dr. Nye:

Not in humans. I mean, we see that women will take an omega-3 supplement. I don't think we really understand all of the impact it can have. Specifically, in the breast, we think the omega-3 fatty acids have become part of the lipid membrane in our cells and that decreases some of the activity of some pro-cancer mechanisms and so that is the thought behind the omega-3 supplement in reducing the risk of breast cancer. But, you're right, there's a lot still to be understood and that we hope to figure out with looking at different biomarkers.

Dr. Birnholz:

Fascinating and I'm definitely gonna want to ask about some of the serum biomarkers, because I believe your study monitored some of them.

Dr. Nye:

We looked at serum biomarkers; it was not the primary or even really the secondary endpoint for the study, so it's really just exploratory. We reported that women had very low omega-3 levels to start, which went along with the nutritional assessments that they also reported. So, remember we're in Kansas, we are meat and potatoes, no bodies of water around us and women had very low intake of omega-3, and that's what their serum level showed, and then we showed that they were compliant with the supplement. Their levels went up nicely with six months of a moderate dose of omega-3 supplementation.

Dr. Birnholz:

And does the route of administration matter in this regard? I take it it wasn't simply pop a pill in the case of the study...

Dr. Nye: It was.

Dr. Birnholz: Was it?

Dr. Nye:

It was. It was actually a generic form of the cardiovascular supplement Lovaza and it contains EPA and DHA, so two types of omega-3 fatty acids, and they were asked to take two pills a day. We are looking at different routes of omega-3 supplementations, still oral routes but different ways of delivering that that may have even better absorption.

Dr. Birnholz:

That's great. I was curious about that because with respect to trying to monitor for breast cancer risk and any kind of mitigation there, the question may come up whether a systemic route of administration would – certainly it's the most intuitive and easiest way to administer, but would something more localized or direct, such as fatty acid injections, be needed in order to help compound that risk mitigation.

Dr. Nye:

I think the biggest thing that I took away from our feasibility study is women want the least invasive route of intervention, of study, and especially this age of women, and so I think there are some new techniques out there to deliver medications orally with better absorption and so that is the direction I'm currently headed. I have not heard of any topical methods for delivering omegas, although we are looking at that with some of our other chemo prevention agents and so that'll be interesting to see some of the questions that have come up. Can that be delivered to younger women? Would that be safe in pregnancy? What is the systemic absorption of those deliveries of drugs? But I think the less invasive we can be, the better.

Dr. Birnholz:

Yeah and to probably put it in another way, it's likely, based on what you found, a non-starter if you're going to recommend invasive routes for many patients, given the idea of reducing risk but not necessarily facing the diagnosis itself.

Dr. Nye:

Correct, these women do not have breast cancer and so their need is different. They may be at high risk for breast cancer, but their motivation comes from a risk not a diagnosis.

Dr. Birnholz:

And to come back on the patient demographics for your study, in particular, there was a wide range of demographics, if I'm not mistaken, regarding pregnancy histories, genetic risk factors for breast cancer and even family histories for breast cancer. Is that right?

Dr. Nye:

Uh-huh. So, approximately half of the women had had a prior pregnancy, half were still desiring a pregnancy, and about 40% had had a family history of breast cancer, and about 40% had had a genetic mutation that is associated with increased risk of breast cancer. So, these are motivated women, and I think that's why I'm so interested in studying them is because they're there, they want to take action in their generation that's really interested in reducing the risk of breast cancer now.

Dr. Birnholz:

And on that note, what did you discover at this point? It's early yet. There is more work to be done. But what did you discover? What new insights can you put on the table?

Dr. Nye:

I think that this is a cohort of patients that needs more attention. I think we need to be looking at not only chemo prevention for this

population, but also lifestyle modifications, which we're working on. And then, that they're interested and willing to participate in trials, and so we need to bring those to them. And then, we need better biomarkers. So, we need less invasive biomarkers. Right now, we're using the RPFNA which is a fine-needle aspiration of the breast, or in some studies, they'll use core-needle biopsies of the breast to collect tissue, and that is really the only means that we have reliable biomarkers in these premenopausal women. And so that's why the study collected stool, urine, serum, as well as breast tissue to try and see what may be feasible in this premenopausal population because we're up against the hormone fluctuations, we're up against high breast density on mammography, and so our typical potential biomarkers that we may use in other cohorts of high-risk women aren't as feasible. I'm really looking forward to seeing the microbiome biomarker that we collected, which we don't have yet, and we're looking at it in the stool as well as the breast tissue, and I'm hoping to see some exciting changes with the supplement there.

Dr. Birnholz:

Well, it sounds like you're moving towards a larger-scale prevention trial. Would that be a good assessment of where you're headed?

Dr. Nye:

That is the goal, yes. I first wanted to prove that women were interested, willing, and that we may have a hint at some biomarkers we can look at in future studies, but I would like to see this expand to a larger study.

Dr. Birnholz:

So, Dr. Nye, any closing thoughts? We've looked ahead. We have a good sense of where the next research directions could be. Any other thoughts that you might want to offer to our health care professional audience around this subject, which is complex? There are a lot of factors here.

Dr. Nye:

I think this younger generation of women are really interested in their breast health. They want to know what is their risk of breast cancer and what they can do about it, and for primary care physicians, the family physicians, internists, OB/GYNs, this is a population of patients who really wants to know and so helping to educate them simply just on the risks so they can seek the resources to better understand what they can do to reduce their risk.

Dr. Birnholz:

On that note, I very much want to thank my guest, Dr. Lauren Nye, for joining me to walk through the findings of her feasibility study on omega-3 supplementation for women at high risk for breast cancer and who are considering future pregnancy. Dr. Nye, it's fantastic having you on the program.

Dr. Nye: Thank you, again.

Dr. Birnholz:

For access to this and other episodes covering innovations in breast cancer research and treatment, visit [ReachMD.com](https://ReachMD.com), where you can be part of the knowledge. For ReachMD, I'm Dr. Matt Birnholz, and thanks for listening.

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