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Medical Management of Endometriosis: GnRH Antagonists

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Medical Management of Endometriosis: GnRH Antagonists” is provided by Omnia Education.

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Dr. Shulman:
Over the last few years, oral GnRH antagonists have transformed the management of endometriosis. Evolving treatment means that we should no longer be recommending surgery to diagnose and manage this condition. It really is the dawn of a new day.

This is CME on ReachMD, and I'm Dr. Lee Shulman. I'm joined today by Dr. Andrea Lukes, founder and CEO of Carolina Women's Research and Wellness Center in Durham, North Carolina, who is a true national expert recognized for her research on endometriosis, contraception, and women's health.

Andrea, it's great for you to be with us today.

Dr. Lukes:
Thank you, Lee.

Dr. Shulman:
Could you provide us with a brief overview of how the approach to endometriosis has evolved over the last several years?

Dr. Lukes:
Certainly. So we've seen a shift. The shift is towards medical management. Clinicians are considering surgery for endometriosis, but oftentimes it's later in the management algorithm. The shifts in management strategy during the pandemic certainly changed many of our practices, and oftentimes management can be done through telehealth appointments. We still rely, of course, on history taking, pelvic exam, diagnostic imaging, usually starting with ultrasound, if an adnexal mass is seen, perhaps an MRI or a CT. And then, of course, many of us are surgically minded and consider laparoscopy depending on a woman's needs. But as you mentioned, the GnRH antagonists are now providing us with new management strategies.

Dr. Shulman:
Even with the evolution of our approach to endometriosis there are still some old-school issues that I think all clinicians need to embrace. And that is, first of all, we truly need to carefully listen to our patients and to really understand what they're looking for, what is the clinical outcome, whether it's fertility or pain reduction. And really, we need to be aware not just of her needs and desires, but what tools we now have to potentially make that happen. That shared decision-making is going to really make or break our success in helping this patient achieve her outcomes.

Andrea, what's the most notable change to how we should be approaching endometriosis?

Dr. Lukes:
Well, so let me just say how much I agree with shared decision-making. And I often emphasize to my patients that endometriosis is a lifelong condition. Oftentimes, you know, you'll use medications but then may need surgery, then may change medications. It's something that can happen really throughout a woman's reproductive years. There is some duration of use limitations with the GnRH antagonists, but I think as we use them more and as more data grows, that may change. I think this new option of the GnRH antagonists is really exciting for women's health.

Dr. Shulman:
There are a couple of things that really have, for me as a clinician, been the hallmark of the challenges with endometriosis. Even as early on as medical school, I was taught that doing surgery for patients with pain is invariably not a good approach. Obviously, there are some patients who need a surgical intervention. But one of the problems with endometriosis is that, until recently, surgery was in fact the primary approach. And it frequently did not provide the patients with the outcomes that they desired.

In addition to the development of the GnRH antagonists, the realization that what had been the conventional therapies, whether it was continuous hormonal contraceptives or progestin-only methods, did potentially work for some patients, but in general, again, did not provide the kind of clinical outcomes that our patients were truly seeking.

So I think as you've just well stated, endometriosis does not need to be a primarily surgical disease, both from a standpoint of diagnosis and treatment, except for certain particular conditions like adnexal torsion or large endometrioma, that we now have very good or excellent approaches to medical management for these patients that can potentially provide them with the clinical outcomes that they seek without having to take that patient to the operating room.

Well, let's now put this into context for our listeners. Andrea, what does and does not work based on your clinical experience? For example, again, as I said previously, many clinicians used either continuous combination methods or progestin-only methods, such as Depo-Provera, and the literature was rather clear that, except for some patients, in general, these regimens did not work well.

Dr. Lukes:
That shared decision-making that you mentioned is important. It's a lifelong condition. So listening to our patients is so important to understanding which direction to take. Agree birth control pills as combination pills can work for certain patients. And when they do, that's great. But in my experience, there's limitation there because often it's an estrogen-dominant disease, and it doesn't always work. It may work for a short term, but then other options may be required. GnRH antagonists, I think, are so exciting. Their indication for moderate to severe disease associated with endometriosis is impressive. There are further ongoing clinical trials on these as contraception or combining the GnRH antagonist with a birth control pill. So I think as we get that additional information, that's something for us to look forward to. But clinicians sometimes need to consider certain methods of contraceptions, if that's not part of the GnRH antagonist label, and that's important to consider.

Dr. Shulman:
What you just said is so true. While, obviously, combination oral contraceptives and combination contraceptives, oral or non-oral, clearly inhibit ovulation – and inhibition of ovulation is what leads to contraception and potentially to an improvement in endometriosis – it is still an estrogen-dominant condition. And in getting to that ovulation inhibition, you're still providing a very long-acting estrogen molecule that I think after the short term is, really for a lot of women, stops providing the benefit that they seek.

And I think what our listeners need to understand is that we now have, in GnRH antagonists, methods that are clearly superior to conventional contraceptives for providing pain relief and providing ongoing management of this lifelong condition. So many of our colleagues are a bit standoffish in taking on new interventions. They want to first see how certain of their colleagues are doing with these methods before they start. But in failing to take on and use GnRH antagonists, our clinicians are really avoiding a far better medical intervention. I think it's programs like this that will hopefully bring this information to a wider swath of women's healthcare providers.

I use GnRH antagonists right now as a first-line therapy. Now that took me a few months to start changing over, and obviously there are some patients for whom hormonal contraceptives may still make sense, but in combining barrier methods and perhaps nonhormonal methods of contraception with GnRH antagonists, I feel for that woman who has endometriosis and symptomatic endometriosis and who doesn't want to get pregnant, I have the ability now to have a superior medical intervention as well as providing effective contraception.

For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Lee Shulman, and here with me today is Dr. Andrea Lukes. We're turning now to practical tips for managing endometriosis.

Andrea, can you provide our listeners with some practical tips for the management of endometriosis? For instance, how do you address contraindications?

Dr. Lukes:
Well, so I think the first step for providers is to consider the diagnosis of endometriosis. It impacts 10% of the population overall. But in women with pelvic pain, it's up to 50%. And with women having infertility, it's up to 70%. So I think it's very important for us to consider the diagnosis probably more than we have in the past, especially given the new emerging treatments.

Endometriosis can impact all socioeconomic and ethnic groups. So in some ways, it's kind of an equal opportunity disease. And then clinicians need to consider when a woman mentions her menstrual bleeding is heavy, they need follow-up questions. They need to understand if the woman has cramping with her periods or dysmenorrhea. Does she have non-menstrual pelvic pain? Does she have pain with intercourse? I start with GnRH antagonists. And I agree with you; I think it is a first-line therapy. The benefit to the woman is seen early on. The pain reduction occurs by 4 to 8 weeks. So that's when I like to bring patients in. So if I start a GnRH antagonist, I encourage them to come back in 4 to 8 weeks, because I think they'll see the benefit. And then I want to look at any side effects they might have. Is there an impact on mood? And then if, in general, in my experience – including the clinical trials, I've used the GnRH antagonists for over 10 years – most women feel benefit by 4 to 8 weeks. And at that time, I'll address vitamin D and calcium, encourage that use if we think someone's going to use it long term. Bone density is certainly a consideration. So I think that needs to be addressed with the supplementation of vitamin D and calcium.

Dr. Shulman:
I think both of our excitement about GnRH antagonists has to at least be presented in the context that no one intervention or therapeutic option, even if it actually is highly effective, is going to be appropriate for every patient, whether it's contraindications, as you've mentioned, whether it's the way the patient reacts to using it, it clearly is not a magic pill. And there are some women who either shouldn't be put on it, or some women who are put on it who are going to have side effects or not the desired clinical impact.

We have to maintain our abilities as clinicians, whether we're physicians or nurse practitioners, to make sure that the patient is doing well with the regimen, is using it properly, and does not either have contraindications to its use or adverse events from its use.

Andrea, before we wrap up, what's your take-home message for our audience?

Dr. Lukes:
I want our colleagues and providers to consider GnRH antagonist as first-line therapy. The effectiveness warrants the first-line therapy. The shared decision-making, as you mentioned, is so important, and you have to consider where a woman is in her life span. Is she in her 20s and needs birth control? Is she 40, done childbearing, et cetera? Certainly, I think the GnRH antagonists can be considered in each decade of life. Similar to fibroids, some people limit the use or think of it only as a bridge to menopause or potentially pregnancy, but I think it's appropriate in the 20s, 30s, and 40s.

The other thing I'd say is I don't think a woman needs to fail a therapy before considering the GnRH antagonists. There's such good evidence to show its effectiveness. I don't recommend a combination birth control pill or a progestin-only pill before I would consider a GnRH antagonist. I don't think, as we mentioned earlier, you have to do surgery before you would use a GnRH antagonist if you have that clinical suspicion of endometriosis.

And then lastly, as I mentioned, I think where a woman is in her reproductive plans certainly impacts the decisions you make with your individual patient.

Dr. Shulman:
You know, Andrea, I could not agree with you more.

The introduction of these medications has changed the approach, the surgical medical approach to this condition. It does not mean that surgery is never going to be an option anymore or isn't even necessarily going to be a primary option. For some women, it is still going to be needed and an appropriate approach. However, our colleagues need to understand that these drugs do provide a superior approach to pain relief and treatment of endometriosis. And it has changed the algorithm by which we're going to evaluate and treat patients with endometriosis.

Unfortunately, that's all the time we have today. So I want to thank our audience for listening in, and I want to thank you, Andrea, for sharing your expertise and insight. It was absolutely wonderful speaking with you today.

Dr. Lukes:
Thank you, Lee. You're one of the true worldwide experts so I appreciate the opportunity.

Announcer:
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