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# Medical Management of Uterine Fibroids and Endometriosis: The Emerging Value Proposition Surrounding the New Oral GnRH Antagonists

Announcer:
Welcome to CME on ReachMD. This activity, entitl*ed "*Medical Management of Uterine Fibroids and Endometriosis: The Emerging Value Proposition Surrounding the New Oral GnRH Antagonists" is provided by Omnia Education.

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Dr. Shulman:
This is CME on ReachMD, and I'm Dr. Lee Shulman. In our practices, we see many patients seeking symptomatic relief from their uterine fibroids and/or endometriosis. Today I will be discussing the role of medical management for both of these troubling conditions with Dr. Andrea Lukes. Dr. Lukes, welcome to the show.

Dr. Lukes:
Thank you, Dr. Shulman. Good to work with you again.

Dr. Shulman:
As always, same here. Let's dive right in. Dr. Lukes, can you briefly describe the quality of life and psychosocial burden for women who suffer from uterine fibroids or endometriosis?

Dr. Lukes:
Uterine fibroids can impact 40% of women in their reproductive age, and by the time a woman is 50, 70%-80% of women are impacted by uterine fibroids. One in four are symptomatic. The symptoms can range from bleeding symptoms, with or without anemia, bulk symptoms where a woman may feel pressure or heaviness in her pelvis. Fibroids are associated with pain, urinary, bowel symptoms, fertility. So it's a common problem and the psychosocial, quality of life measures are important to consider.

So I'm familiar with kind of a standardized, validated, disease-specific tool called the Uterine Fibroid Symptom Quality of Life. It's been used with these new GnRH antagonists on the market, but as well as with uterine artery embolization, radiofrequency ablation of fibroids, and other treatments for fibroids. It has 2 different measures. There's a symptom severity, including 8 items, there's 29 items in this health-related quality of life measure. But the important domains, and there are 6, are a woman's activities, her concerns, energy and mood, control, self-consciousness, and even sexual function. So fibroids and associated symptoms can truly negatively impact a woman's quality of life.

When you look at endometriosis then, again, 10% of the population has endometriosis, and higher percentages are seen in those women that have pain and infertility. The symptoms typically are, as I mentioned, pain – and there are 3 types: dysmenorrhea, non-menstrual pelvic pain and dyspareunia, and then infertility. And again, there are disease-specific quality of life measures. The one I'm most familiar with is the EHP-30, or Endometriosis Health Profile, and there are 30 questions with this, and there are 5 core scales, and those look at pain, control and powerlessness, emotional well-being, social support, and a woman's self-image. So both disorders can

have a negative impact on a woman's quality of life.

Dr. Shulman:
Andrea with that sobering background on the burden faced by women suffering from uterine fibroids or endometriosis, which patients do you think are suitable candidates for medical management, and who are not?

Dr. Lukes:
Fibroids are still the most common indication for having a hysterectomy, but these are both disorders in women that impact them for decades over their life. So unless there is a contraindication to medical therapy, like someone has an increased risk of thrombosis, has a personal history of thrombosis, you know, or has debilitating migraines with auras, if there's not a clear contraindication to medical management, then I think providers should consider medical management for the majority of women. I'm hopeful that with these new GnRH antagonists, providers will embrace medical therapies for most people.

Dr. Shulman:
You know, when I see a patient with symptomatic fibroids or endometriosis, I essentially tell them that surgery is going to be the last option. We may get there, and unfortunately, we do get there at times.

Now, Andrea, can you tell us about the currently available types of medical management for uterine fibroids and endometriosis? And what are the advantages and disadvantages of some of the more common options?

Dr. Lukes:
Sure, and there's a lot of overlap between treatments for fibroids and endometriosis, but it does depend on the symptoms, so certainly you want to choose a medical therapy that addresses a woman's symptoms. So for fibroids, if her symptoms tend to be bleeding, probably the most common one we're used to are the combined oral contraceptives. But we have the progestin-containing IUDs, or intrauterine systems, tranexamic acid – big supporter of tranexamic acid, which is nonhormonal. You only take it during the menstrual cycle. You know, we've had GnRH agonists, and now these GnRH antagonists can be used longer term, both available medications, one using elagolix, one using relugolix. Both have an indication of heavy menstrual bleeding associated with fibroids. And then, still in research development, there are other medications including aromatase inhibitors, the selective progesterone receptor modulators, et cetera. And then, bulk symptoms – I do prefer those GnRH antagonists or agonists, which can cause reduction in uterine volume.

Endometriosis, usually if you're going to address pain, then you have different pain medications. Non-steroidals, you can consider opioids, but of course there's a, you know, addictive issue with opioids. But we've used progestin-only contraceptives, the combined oral contraceptives, androgens, and again, those GnRH agonists, and then the newer GnRH antagonists provide a good option for women with pain associated with endometriosis.

Dr. Shulman:
You know, I can't agree with you more.

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. Our focus is on the role of medical management in the treatment of uterine fibroids and endometriosis.

But, you know, we've mentioned now several times the GnRH antagonists, so let's focus on them. Can you specifically discuss their mechanism of action, the clinical data that surrounded their approval, as well as any real-world evidence – as well as where they fit into current guidelines for uterine fibroids and endometriosis?

Dr. Lukes:
Yes, so I'll mention, you know, the statement papers by ACOG and ASRM address endometriosis as a medical condition. So it's exciting to have both elagolix compounds and relugolix as GnRH antagonists to treat pain associated with fibroids, as well as indication for heavy menstrual bleeding associated with fibroids. Then there's a newer one, linzagolix, that's being developed. But the 2 on the market now include the elagolix-containing compound and the relugolix. They do have different half-lives. Elagolix is 4 to 6 hours; relugolix is longer – 25 hours. But a GnRH antagonist – it's a compound that competes with a woman's endogenous GnRH, subsequently lowering the ovarian production of estrogen and progesterone. And they don't lower it to the point where you have none. They lower it to a threshold in which pain with endometriosis improves, as well as heavy menstrual bleeding associated with fibroids improve.

So then when you're lowering a woman's FSH, LH, estrogen, progesterone, she can have side effects related to that. So there's a combination therapy or a replacement therapy, however you want to use the terminology, that estradiol and norethindrone acetate are given with elagolix, in particular, ORIAHNN. And then with Myfembree – the brand names of these compounds, to mitigate bone loss as well as improve vasomotor symptoms or estrogen deficiency-associated hormones.

And then, when you look at the clinical trials on reducing heavy menstrual bleeding associated with fibroids, for instance, you know, the

FDA-designed trials for elagolix and relugolix were very similar, the primary outcomes being a reduction below 80 milliliters of menstrual blood loss, which is the definition of the historical term “menorrhagia,” which is now termed “heavy menstrual bleeding.” And in addition to lowering it below 80 milliliters, you have to have a 50% reduction from baseline to 6 months. They both have in the phase 3 trials a 6-month duration. And similar results, basically. Over 70% of women were responders and had reduction in heavy menstrual bleeding associated with fibroids.

Similarly, the results in the endometriosis studies, you see marked reduction in the types of pain that women experience with endometriosis. The dysmenorrhea, non-menstrual pelvic pain, and then in some instances, dyspareunia. And what I also like about the compounds is they work quickly, so when I prescribe GnRH antagonists [elagolix or relugolix], I will bring women back 4 to 8 weeks after starting therapy, because the benefit occurs early, and I want to address any adverse reactions a woman may have. They lower estrogen and progesterone within a day or 2, but if you stop them, they return to normal levels very quickly, so those side effects or adverse reactions go away quickly.

Dr. Shulman:
Andrea, many of our colleagues provide care to their patients using guidance from the American College of Obstetricians and Gynecologists. Can you just briefly address where the GnRH antagonists fit within the most recent guidelines that have been published by ACOG?

Dr. Lukes:
Yes. So that came out just this summer – June, I believe, in 2021, and it’s considered, really, first-line therapy. It should be considered as one of the first options we give women. So my approach in medical management of heavy menstrual bleeding and fibroids is to go over the comprehensive options, but few really are used on-label or in an FDA-approved indication.

So now we have 2 options [elagolix or relugolix] that are indicated for heavy menstrual bleeding and fibroids, and that’s exciting. And I was pleased to see that ACOG, in their new bulletin, supported the use of GnRH antagonists early on in treatment.

Dr. Shulman:
I will echo that satisfaction. All too frequently, guidelines lag considerably in time behind the development and introduction of new options, and I really do give ACOG credit for bringing these primary indication, therapeutics, not just as a part of the armamentarium that we should be using, but as a first-line, mainstream option.

Dr. Lukes, I want to thank you for that deep dive into GnRH antagonists with uterine fibroids and endometriosis. Is there anything else that you would like our listeners to know that we haven’t already touched upon in today’s discussion?

Dr. Lukes:
Dr. Shulman, there’s certainly a role for surgery, but the GnRH antagonists, they’re exciting and safe medications. So I think prescribing these medications are going to benefit a woman long-term over many reproductive years for both heavy menstrual bleeding and fibroids as well as endometriosis. I’m hopeful that our colleagues will begin to prescribe GnRH antagonists.

Dr. Shulman:
You know, I can’t agree with you more. I think that’s where the role of ACOG plays such an important factor in this, recognizing that these GnRH antagonists do play a first-line, mainstream option, not just as add-on, potential off-label use, but as an on-label approach to successful treatment of the symptoms of uterine fibroids and endometriosis.

Andrea, unfortunately, that’s all the time we have today, so I want to thank our audience for listening in, and thank you, Dr. Andrea Lukes, for joining me and for sharing all of your valuable insights. It was great speaking with you today.

Dr. Lukes:
You, too. Thank you for having me on.

Announcer:
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