

Transcript Details

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ReachMD

www.reachmd.com
info@reachmd.com
(866) 423-7849

Menopause and Bone Health: Modern Approaches for Healthcare Providers

Announcer:

You're listening to *Boning Up on Osteoporosis* on ReachMD, sponsored by the Bone Health and Osteoporosis Foundation. Here's your host, CEO of the Bone Health and Osteoporosis Foundation, Claire Gill.

Claire Gill:

Welcome to today's episode, navigating Menopause and Bone Health Modern Approaches for Healthcare Providers. We are excited to be joined by Dr. Andrea Singer, Chief Medical Officer of Bone Health and Osteoporosis Foundation, professor of Medicine and Obstetrics and gynecology at MedStar Georgetown University Hospital, and a member of the National Menopause Foundation's Medical Advisory Committee. Dr. Singer is a leading authority on women's health, bone health and osteoporosis. Dr. Singer, welcome to the program.

Dr. Andrea Singer:

Thanks so much for having me, Claire.

Claire Gill:

So, we're excited that, in this episode, you're going to guide us through the intricate connections between menopause and bone health. We'll explore how menopause, which is a natural yet significant transition in women's lives, brings about hormonal changes that can lead to a range of symptoms including vasomotor disturbances, sleep disruptions, and mood fluctuations. Importantly, we'll also discuss the profound impact these changes have on bone health, particularly the accelerated bone loss that increases a woman's risk of osteoporosis and fractures. Dr. Singer will share evidence-based strategies for managing menopause symptoms and maintaining bone health, emphasizing the benefits and risks of menopausal hormone therapy and effective non-hormonal options. With women now living decades beyond menopause, it's vital for healthcare providers to understand the connection between menopause and bone health to better support their patients. Whether you're looking to refine your approach or stay current on best practices, this episode promises to be an invaluable resource. So let's get started. Dr. Singer, can you define menopause and explain the key physiological changes that occur during this transition?

Dr. Andrea Singer:

Before I answer the first question, I just want to acknowledge upfront that during this discussion I may use gender specific language as reflected in the clinical papers, studies and publications that I may also reference. I do recognize that some individuals may identify differently than the gender and pronouns that I use. With that said, happy to define menopause, which is a natural physiologic event. If we as women live long enough, we'll all go through menopause. It's defined though technically as the final menstrual period and is actually a retrospective diagnosis, meaning that we know it's menopause after a year without periods or menstrual bleeding. What menopause actually represents is the permanent cessation of menses- one no longer having periods- which results from loss of ovarian follicular function. Usually this is because of aging, but sometimes can happen because of surgery or something else. And this loss of ovarian function results in a decline in ovarian estrogen, actually, estrogen and progesterone and those declining levels are really the impetus or factors that contribute to many of the symptoms you mentioned in the introduction. Couple of quick numbers, if you will. The median age of menopause in the US is 52.5, and I think it's really important for us to think about the fact that women worldwide are living longer. So many women will spend 40% or more of their lives in the postmenopausal period, and more than 60% survive until at least the age of 80. So we have to think about all of the factors that occurred during the transition and also throughout the remainder of one's life without estrogen around.

Claire Gill:

So you mentioned again the symptoms that we spoke of in the introduction, but let's dive a little deeper into what are the common symptoms of menopause and what influences the experience of these symptoms?

Dr. Andrea Singer:

That's a great question. First of all, there's no one universal menopause syndrome or symptom. The experience for each woman can be very different, but vasomotor symptoms, what we commonly refer to as hot flashes and or night sweats are the most common and bothersome symptom of menopause, and they are experienced in up to 80% of women. Other systems though that are affected and associated symptoms that can come with that are the central nervous system. That includes things like sleep disturbances, an increase in migraine headaches, mood changes, both depression and anxiety and cognitive changes, which our patients may sometimes call brain fog, and effects in the cardiovascular system. So there can be changes in cholesterol profiles and an increased risk of heart disease at this time of life and beyond. Sexual health changes, probably most commonly decreased desire or hypoactive sexual desire disorder, genitourinary syndrome of menopause sounds like a mouthful, but we're talking about things like pain with intercourse, vaginal dryness and burning, sometimes an increase in urinary symptoms and infections as well as incontinence. Those dreaded metabolic changes and weight gain, which often occurs sort of in the mid part of the body. Arthralgia and arthritis -so bone aches and pains, fitting into what has recently been termed the musculoskeletal syndrome of menopause. And something that is very near and dear to my heart in a major area interest of mine, which is bone loss and osteoporosis, and we'll talk a little bit more about that. The interesting thing is that the occurrence and severity of menopausal symptoms varies widely and they're influenced by multiple factors including race and ethnicity, comorbid conditions, so other medical problems that someone might have as well as psychosocial and socioeconomic factors. Just to kind of illustrate this, we have data from the SWAN study or Study of Women's Health Across the Nation that looks at the average duration of vasomotor symptoms, which in all comers is 7.6 years, but there's a difference in white women that average duration is six and a half years. In Hispanics, 8.9 years in blacks, 10.1 years. So this isn't something to just grin and bear for a couple of months and it goes away. And just to sort of round that out and Japanese and Chinese women, shorter duration between 4.8 and 5.4 years respectively. So no one size fits all, and we have to realize that symptoms can impact the quality of life, including mental health, wellbeing, relationships, work productivity, and I'm sure everyone listening could add to this list.

Claire Gill:

Well, it's no wonder that both women and their clinical providers are so confused around this stage of life, given how much really can happen, as you said, depending on the individual and what they're experiencing. But let's now dive in a little bit again, as you said to something near and dear to your heart around the influence of menopause on bone health. What are the implications for osteoporosis management in post-menopausal women?

Dr. Andrea Singer:

Estrogen deficiency is the main pathophysiologic mechanism, if you will, behind the bone loss that occurs at menopause. And menopause has been termed by some as the defining event in the development of osteoporosis for this reason. If we take a step back for a second, we need to realize that bone density at any given age is a function of both peak bone mass, so how much you put into the bank, which is generally reached by about the age of 30 and how much bone is subsequently lost or how much you withdraw. Over the menopause transition, women can lose 10 to 12% of their peak bone mass, which if you're looking at bone density measurements translates into approximately a loss of one T-score. Women lose as much bone mass during the menopausal transition as they do from then until about the age of 80. And if you think about it, women who come to menopause with low mass or less in the bank develop osteoporosis earlier and sometimes by their mid-sixties. The good news is consistent improvement in spine and hip bone density has been seen with the use of estrogen or treatment with hormones in multiple studies. We know that the magnitude of the effect that we see is based on estrogen dose, so osteoporosis can be prevented and hormones clearly have a role, but therapy really needs to begin during this perimenopausal transition, or at the time of menopause. If we think about that and do that when appropriate, the accelerated bone loss that would occur is prevented and the underlying trabecular microarchitecture or how well connected the bone is, that structure is maintained. We'll talk about this a little bit more in a few moments, but the safety profile, particularly in terms of cardiovascular safety is much better when estrogen is started earlier as opposed to when it is started later, so there are lots of things for us to think about as women are going through menopause. We do need to keep in mind that at some point if one stops using hormones, if they've chosen to treat with estrogen that there's a loss of bone density and fracture protection when estrogen is stopped. So, because this is a chronic condition, one then needs to think about transitioning to something else to maintain the bone density builds or maintenance that might have been seen.

Claire Gill:

For those of you just tuning in, you're listening to *Boning Up an Osteoporosis* on ReachMD. I'm Claire Gill and I'm speaking today with Dr. Andrea Singer about menopause and bone health. Dr. Singer, let's go back again and talk a little bit more about menopause

hormone therapy that you just mentioned. What are the current recommendations for it and how have they evolved over the years in light of research findings?

Dr. Andrea Singer:

The main indications for using menopausal hormone therapy- which would be estrogen alone in somebody who has had a hysterectomy, estrogen in combination with a progestin in someone who still has a uterus- we'll just sort of refer to it as hormone therapy. Main indications or treatment of symptoms and the prevention of osteoporosis and postmenopausal women who are at increased risk for osteoporosis. If one is interested, the current recommendations are nicely summarized in the 2022 North American Menopause Society, now the Menopause Society, their position statement on hormone therapy. Essentially what it says is that when hormone therapy is initiated before age 60 or within 10 years of menopause for the treatment of symptoms, the benefit risk ratio for the use of hormones is favorable. What we used to think about the guidance being in terms of the lowest dose for the shortest period of time has been replaced with the appropriate dose by the appropriate route for the appropriate length of time to reach one's treatment goals. So the emphasis on this now is really on individualizing therapy and the recommendations are largely based on assessing patient risk for potential complications. In other words, assessing for risk of breast cancer and cardiovascular disease specifically, and weighing those risks with the benefit that one might realize from treating with hormones. I think the other thing that one has to realize is we've come a long way from 2002 when the results of the combination hormone therapy arm of the Women's Health Initiative were released, and for any of us who were practicing at that time, we know exactly where we were when phones started ringing off the hook with questions. But there have been multiple reanalyses and published papers, for instance, one looking at breast cancer data at 20 years of follow-up post randomization, others looking at all cause pooled mortality hazard ratios at 18 years of follow-up based on age of randomization, and we've learned a lot about that benefit risk perspective from these additional studies. Overall, the increased absolute risks associated with hormone therapy are pretty rare, less than 10 per 10,000 years of treatment and include increased risk for venous thromboembolic disease, deep venous thrombosis or blood clots in the legs, pulmonary embolism as well as gallbladder disease. Estrogen and progestin therapy carries a pretty rare but increased risk for stroke and breast cancer. That's in the combination arm for breast cancer. And if one were to give estrogen without progestin in a woman who has a uterus, then we have to certainly worry about the risk of endometrial hyperplasia and cancer. But we don't do that. But it's important to also realize that we've seen that the absolute risks are reduced for all-cause mortality or death. For fractures, right, highlighting the bone relationship again, diabetes, breast cancer in the estrogen only arm, and so many important things are actually reduced when hormone therapy is started in women under the age of 60.

Claire Gill:

Good to know that the efficacy of hormone therapy is very high while the risks are seen to be lower, but for those who aren't able to take hormone therapy, can you discuss a little bit about non-hormonal options for managing menopausal symptoms and in which scenarios are those preferred over hormone therapy?

Dr. Andrea Singer:

Well, as you mentioned, we tend to think about non-hormonal options if a woman has a contraindication to hormone therapy and there are a list of contraindications, but just to give a couple of examples, if one has a current diagnosis or suspected diagnosis of breast cancer or a history of breast cancer, that may be a contraindication. Other estrogen sensitive malignancies, undiagnosed genital bleeding, a history of venous thromboembolic disease, deep venous thrombosis or pulmonary embolism, those are often contraindications and there are others as well. So in the setting of comorbidities that would lead us to not use hormones, non-hormonal therapies can be considered. And sometimes, or for some women, they don't want to take hormones and they would like a different approach. So those are sort of the general categories where we think of the use of other agents. There are only two FDA-approved non-hormonal medications at this time. One is a specific form of paroxetine, which is a selective serotonin re-uptake inhibitor or SSRI, and we'll come back to that in a moment. The other is a medication called fezolinetant, which is a first in class neurokinin B antagonist. Sounds like a mouthful. Let me back up for a little bit and talk about how that works. And I mention this because this is sort of the newest kid on the block, if you will. There are KNDy neurons, KNDy standing for kisspeptin neurokinin B and dynorphin neurons, which are estrogen sensitive neurons found in the hypothalamus, which can become hypertrophied in menopause and are a link between estrogen decline and vasomotor symptoms. In essence, there's a dysregulation that's caused by declining estrogen, which normally inhibits the activity of these neurons and unopposed binding of neurokinin B, which generally increases stimulation of these neurons. And when they're no longer in sync, that leads to increased activation of the heat dissipation mechanisms. So there's hypertrophy of these neurons, they send signals to the thermo regulatory center. There's increased vasodilation, sweating and all the classic symptoms, vasomotor symptoms. Fezolinetant blocks the binding of neurokinin B at its receptor and moderates this neuronal activity helping to restore that thermo regulatory balance. So this is a first in class newer drug. There is another one that is currently in development as well, but Fezolinetant and this particular form of paroxetine are the two FDA approved medications. With that said, off-label, we have experience with and certainly use other agents as well, other SSRIs and SNRIs, gabapentin and oxybutynin have all

been used in this setting, and I don't want to forget about the use of non-medication, pharmacologic strategies. There is another position paper from the then North American Menopause Society now the Menopause Society from 2023 reviewing non-hormone therapy for menopausal symptoms. And it really speaks to the evidence that we either have or that we lack with many of these therapies, both those that are not approved behavioral techniques, cognitive behavioral therapy, exercise, not sure that there's a downside to exercise for most, but again, if we're looking to see where data exists, we have to realize that for many of these other strategies, we may not have the same kind of robust randomized controlled trials that we do or that the FDA requires in terms of medications.

Claire Gill:

So given all of that, how do you and how should others approach creating individualized treatment plans for menopausal women who might be facing bone health challenges? And specifically, how do you weigh the risks and benefits of menopause hormone therapy and when do you consider incorporating other strategies for bone health or osteoporosis management?

Dr. Andrea Singer:

Well, I'll wet everyone's appetite because this could be a whole other podcast, but we've talked about the role of estrogen and prevention and management. Although estrogen is only indicated for prevention by the FDA, we do have fracture reduction data from the Women's Health Initiative, as I mentioned earlier. But the approach to bone health really is based on risk stratification and again, individualization of treatment. You sort of hear a theme throughout this. Initial or baseline risk stratification in other words, how high someone's risk for a fracture is helps to inform choice of initial therapy as well as the sequence of therapeutic agents that may be used and also the duration of therapy. We have a number of other medications in our armamentarium from an osteoporosis and fracture reduction standpoint. Two major umbrellas of medicines, if you will, are anabolic or bone building medicines that work primarily to build new bone and our antiresorptive medications that work primarily to slow bone breakdown, although those processes are coupled. So, we in most cases cannot separate them. They all reduce fractures, but there are variable effects on fracture reduction in terms of the sites and the magnitude of that reduction. Variable effects on the degree of bone mineral density effects and increases the rapidity of these changes. And of course the mechanism of action, the benefits and the potential adverse reactions. And so that's why we need to look at each person and try to pick a medication or an initial strategy that is best for them, realizing that this is a chronic disease that we can treat effectively and reduce fracture risk, but we don't cure like other chronic diseases- such as high blood pressure, cardiovascular disease, diabetes- that we need to think about things like the order in which we use drugs, what our goals are. And there are some new papers, a new paper that was just published at the end of August, updating the strategy or focus on goal-directed therapy, and then again, looking at one's response to treatments and realizing that things change as one ages and overall health changes so that this is an ongoing discussion for the long-term between patient and healthcare professional.

Claire Gill:

Well, that brings us to the end of today's program. I want to thank my guest, Dr. Andrea Singer, for joining me to discuss navigating menopause and bone health. Dr. Singer, it was great having you on the program. Thank you.

Dr. Andrea Singer:

Thanks so much for having me.

Announcer:

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