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Advances in Osteoporosis Treatment: Exploring Drug and Non-Drug Interventions

Announcer:

You're listening to *On the Frontlines of Osteoporosis* on ReachMD. And now, here's your host, Ashley Baker.

Ashley Baker:

Welcome to *On the Frontlines of Osteoporosis* on ReachMD. I'm Ashley Baker, and joining me to discuss non-drug and drug interventions for osteoporosis is Dr. Jad Sfeir. Dr. Sfeir is an Associate Professor of Medicine at Mayo Clinic in Rochester, Minnesota, where he holds a dual appointment in the Division of Endocrinology, Diabetes, Metabolism and Nutrition, and the Division of Geriatric Medicine and Gerontology. Dr. Sfeir, thanks for being here today.

Dr. Sfeir:

Thank you for having me.

Ashley Baker:

Dr. Sfeir, let's start by taking a look at non-drug interventions. Which ones do we now consider essential for fracture prevention?

Dr. Sfeir:

There are two interventions that we focus on mainly in what I like to term the osteoporosis prescription. The osteoporosis prescription should start with, first, good nutrition. And these essential nutrients that are important for bone metabolism, as you may know, are calcium and vitamin D. However, appropriate recommendations for calcium and vitamin D are essential, because we see a lot of information that is circulating that may or may not be correct. Typically, we recommend that calcium comes from the diet. Someone who has metabolic bone disorder, specifically osteoporosis, or working on fracture prevention, should target 1,200 milligrams of calcium a day.

The other one, as I mentioned, is vitamin D. Vitamin D—as you know and the listeners know—is the sunshine vitamin, and so vitamin D comes from the sun. Adequate sun exposure varies by latitude, but in general, it's somewhere around 15 to 20 minutes exposure of upper and lower extremities at peak sunshine or peak hours during the day. Supplementation, if we are not able to achieve that, should target about 1,000 international units, or 25 mcg of vitamin D a day.

There has been a lot of recent data that focuses on protein intake and the importance of protein for bone metabolism, and so appropriate protein intake is also essential when we're talking about nutrition for fracture prevention.

These interventions do not necessarily reduce the risk of fracture, but these are the basics—the essentials, as you said—to ensure appropriate bone metabolism so we can keep the bone in a healthy state.

The second thing I mentioned earlier is exercise, and I also mentioned that it is very important to know what type of exercise to do because not all exercise is good exercise for bone metabolism. Even if some exercises are good for cardiovascular health or overall health and they're good to do, they may not impact bone metabolism. The essential for bone metabolism is the basic weight-bearing exercises, and this is something we all know. We tell people to do them all the time, but we need to, many times, go above and beyond weight-bearing exercises, and that is focusing on resistance training and muscle strengthening. These are very important to continue with appropriate bone metabolism throughout the lifespan, particularly because osteoporosis and fracture are typically associated with

older age. So age is the biggest risk factor for fractures, and so as we grow older, we are not only losing bone, we are also losing muscle function. And so muscle training is going to be essential to protect the bone.

And then the last item I would typically mention within the non-pharmacologic intervention is fall prevention. A lot of strategies can be taken in terms of reducing the risk of falling for a patient and subsequently preventing a fracture.

Ashley Baker:

With that being said, what challenges do we see with real-world implementation of these interventions, and what strategies can we use to overcome them?

Dr. Sfeir:

The biggest challenges I see when it comes to nutrition is misinformation. The essentials are calcium and vitamin D. Protein is essential for overall health. There is much more information out there about some other form of supplements that may or may not work in bone metabolism. None of them have shown fracture-risk reduction. And so it is very important to stay away from what is not evidence-based.

Another challenge when it comes to exercise is persistence. I see patients in my clinic. I recommend a certain exercise plan. What I typically do is I go over the big picture when it comes to exercise—the ones that I just mentioned—but many of my patients receive a physical therapy referral. I ask them to meet with a physical therapist in order to get a personalized approach on exercise. However, when I see the patient back in follow-up, many did the first physical therapy recommendation, took the home program with them, and then it stayed on the counter or on the fridge, and it actually never got implemented; or maybe it started by getting implemented for the first few weeks, and then later they dropped that off. And so when we see the patients, let's say, back in the clinic, we should reiterate the importance of exercise and maybe revisit where we are with exercise today, and taking it to the next level before going back and focusing on pharmacologic interventions.

Ashley Baker:

For those just tuning in, you're listening to *On the Frontlines of Osteoporosis* on ReachMD. I'm Ashley Baker, and I'm speaking with Dr. Jad Sfeir about advances in osteoporosis treatment.

So, Dr. Sfeir, let's shift gears and talk about drug therapy now. Can you walk us through the core drug classes used in osteoporosis treatment today?

Dr. Sfeir:

There are two big categories when it comes to medications for reducing the risk of fracture. Bone is going through a turnover or remodeling throughout the lifespan, and the remodeling has two parts. That is bone resorption happening and bone formation happening. And between the two, there is a crosstalk. We call it coupling. There is coupling between bone resorption and bone formation. And so the medications that we use to improve bone metabolism and reduce the risk of fracture are categorized under an antiresorptive that targets bone resorption, and anabolic medication, or specifically osteoanabolic medication, that will target bone formation. And there is a medication—only one right now—that targets both. That is combined antiresorptive and anabolic.

With the antiresorptive, the more common ones and the older medications are the bisphosphonates. For example, we have the oral alendronate or intravenous zoledronate. These are quite common medications that are used to reduce the risk of fracture. Bisphosphonates are the oldest medication. We have very good data, safety information, as well as efficacy information on them. They target resorption by inhibiting the resorption, reducing how much resorption is happening, and allowing the natural bone formation to tip the balance and then improving the bone density and reducing the risk of fracture.

When it comes to osteoanabolic medications, we call them, in general, the bone builders, because they are pushing the bone formation. And so you are getting a significant increase in bone formation and a significant increase in bone mineral density, which translates into very good reduction in fracture risk. There are two categories here. There are the ones that are based on the PTH, the parathyroid hormone. So there is recombinant PTH, and there is recombinant PTHrP, or parathyroid hormone-related peptide. These are teriparatide and abaloparatide. Both of these target the PTH pathway and stimulate bone formation with that.

And then the last one I mentioned, is a combined antiresorptive and anabolic at the same time, is romosozumab, which is a monoclonal antibody against sclerostin. Sclerostin is a hormone that is a much higher level than the coupling that's happening between bone formation and bone resorption, so it is able to impact both by reducing resorption and increasing formation, which will allow for a very good improvement in bone mineral density.

Out of all the medications I mentioned, it is very important to realize that the choice of medication should depend on different

circumstances for different people. And that is, what we term in our clinic, individualizing the choice for osteoporosis medication. The reason for that is because different people are at a different level of fracture risk, and so the higher the fracture risk, the more potent the medication we need to choose in order to reduce the risk of fracture more efficiently and to a better extent.

Ashley Baker:

When it comes to treatment sequencing, how has our understanding and approach shifted in recent years?

Dr. Sfeir:

Very good question. The advances that we had with research and with anabolic agents, as I mentioned—we realized that with anabolics, having them started first gives you the better increment in bone density, and this translates to a bigger reduction in risk of fracture. And so choosing an anabolic first in certain populations is very important before initiating an antiresorptive therapy, because antiresorptive will blunt the increment that will happen with bone density if you were to use it first before anabolic agents.

However, we have realized that we have been treating patients for a long time with antiresorptive agents because these are the more common medications that are used for fracture risk reduction and osteoporosis. And so, in real life, there are many patients that you need to transition from an antiresorptive to an anabolic agent, and so the choice of which one to use will also depend on what is the target is in terms of reducing the risk of fracture, what type of fractures am I trying to target, and what is the increment in bone density I'm looking for is, and that will influence your choice. Even if you had someone on antiresorptive that you need to start anabolic on, then you need to make the choice very wisely based on the current data.

Ashley Baker:

And could you explain what a treat-to-target strategy looks like and how it could help redefine success in osteoporosis management?

Dr. Sfeir:

As I mentioned earlier, individualizing your choice of therapy depends on what your goal is for each different person. And so if your target is a certain type of fracture or your target is a certain T-score you're trying to reach depending on the circumstances of the person, the strategy for sequencing different medication or what to use as a first-line agent will vary significantly. For example, for vertebral fractures, we have very good data on anabolic agents reducing vertebral fractures to a much bigger extent than other agents, and so this may be a good person to use an anabolic agent first. Someone with a very low T-score, particularly a very low T-score at the spine, would be a good example of an individual where you would use an anabolic first before transitioning to an antiresorptive.

Ashley Baker:

Before we wrap up our program, Dr. Sfeir, do you have any final insights you'd like to share with our audience?

Dr. Sfeir:

There are a couple of things that come up a lot in the clinic. When I see individuals who have a very low bone density and the risk of fracture is very high, they're scared of doing any activity or exercise. I started by mentioning that exercise is essential for bone metabolism, and so it's very important to tell our audience that we should not be scared of doing activity or exercise that someone is enjoying because this is part of their therapy. Part of that osteoporosis prescription is doing exercise and staying active. There are, however, limits and margins we may need to tell them. We cannot lift as much anymore. We cannot, maybe, move furniture or lift boxes, but we still need to be active and should not be scared about a low T-score by doing our regular activity and a good exercise plan.

Another thing I wanted to bring up is a lot of individuals are scared of medications. They hear a lot about medications. We talked about misinformation when it comes to nonpharmacologic interventions, but there is even more misinformation when it comes to therapy, and so meeting the person where they are is very important to educate them regarding the safety of the therapy. And again, at the end of the day, we are all working towards fracture risk reduction, and so this is the point of fracture risk reduction for the individual: meeting them where they are and trying to explain why our strategy will include medications. Even if medications come with certain side effects what our strategies to mitigate these side effects are going to be a very important point of discussion.

Ashley Baker:

With those key takeaways in mind, I want to thank my guest, Dr. Jad Sfeir, for joining me to discuss the non-drug and drug interventions available for patients with osteoporosis.

Dr. Sfeir, it was great having you on the program.

Dr. Sfeir:

Thank you for having me.

Announcer:

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