

The Sun is Setting for Sulfonylureas - Frankly Speaking EP 40

Transcript Details

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Dr. Frank Domino:

Marty is a 48-year-old obese male with type 2 diabetes. He works as an accountant and spends his days sitting in front of his computer. While he does not smoke, he is not at all careful with his diet and has no interest in exercise. After finding his hemoglobin A1c at 8.6, you place him on metformin and titrate him up to 1,000 milligrams twice a day. After six months, though, and a trip to the diabetic nurse educator, his A1c still remains quite high at 8.1. In the past, your second choice for this patient would be to use a sulfonylurea, but should we? This is Frank Domino, professor in the Department of Family Medicine and Community Health at the University of Massachusetts Medical School, and joining me today to talk about type 2 diabetes and sulfonylureas is Susan Feeney, assistant professor and coordinator of the family nurse practitioner tract at the University of Massachusetts Medical School Graduate School of Nursing. Welcome to the show, Susan.

Susan Feeney:

Thanks, Frank. So this is an interesting case. What are the risks and benefits of sulfonylureas used with type 2 diabetics?

Dr. Domino:

Up until not that long ago, these were my second choice for meds. They were very effective at lowering A1cs. We didn't have any real data that showed they improved morbidity or mortality

outcomes, but they were fairly simple to use as long as the patient was not at a high risk for hypoglycemia. That being said, a recent systematic review and meta-analysis looked at their role and found some very startling information. The first was that sulfonylurea use increased the risk of cardiovascular-related mortality in all-cause mortality. So here we are, we're using an agent that hasn't been proven to improve any outcomes and actually increases the risk of death. There were higher risks associated for myocardial infarction, when sulfonylureas were compared to some of our newer agents, as well as stroke. So I think, as a class, this group of medications, while valuable from the 60s forward, probably have had their last calling in our care, and I think it's time we rethink their use.

Susan Feeney:

Well, it's interesting 'cause they also are very cheap. And every time I look at the news, there's a new medication out. What are the other options to use when you have either... You don't have this robust a response from the metformin?

Dr. Domino:

Well, when we think of type 2 diabetes, we often think it's a disease of hyperglycemia, but that's our erroneous impression. It's really a disease of insulin resistance. And when you treat insulin resistance, there are only a few things that improve outcomes, the most common of which is weight loss. Decreasing adiposity by just as much as 5% can dramatically improve long-term outcomes in type 2 diabetics who are obese. So my next steps have changed from sulfonylureas to drugs that'll actually have an impact on the patient's weight. So sodium glucose co-transport 2 inhibitors, SGLT-2 inhibitors, are probably my next step, primarily because they're oral, they're once a day, and their risks are very low. They have the potential, in theory, to cause hypoglycemia and urinary tract disorders, but that risk is very, very low.

The real worrisome risk is that in patients with severe peripheral vascular disease they can actually increase the risk of amputations. But that risk is, again, extremely low, but that might be their only severe contraindication. Glucagon-like peptide-1 agonists are also wonderful, but they're given by injection. And both of these classes of drugs have that horrible adverse effect of

being very expensive, so if you're paying out of pocket, they're ridiculous. If you're going to use them, you're going to have to find out what the patient's insurance is, what their formulary prefers, and when they last changed their mind, because I have been using the SGLT-2 inhibitors now for over a year, and come September 1st, the insurers I typically deal with switched to a different preference.

The di-peptide peptidase-4 inhibitors are weight neutral, and so I probably don't think of those as agents I use as second line after metformin, but I consider them. That being said, I would say they're at best third line in my world. I don't ever recommend insulin as a second line primarily because diabetes, especially in obese type 2 diabetic, needs to lose weight and insulin is anabolic. It makes you bigger. It primarily makes you bigger, not by building muscle, but by increasing your fat stores, and that seems counterproductive. We know it does not improve any outcome in type 2 diabetics and makes a number of them worse.

And then TZDs, there was quite a bit of controversy about their adverse effects, and maybe they were increasing the risk of bladder cancer and increasing adverse effects associated with heart failure. I think that data is very nebulous, but these are fourth line drugs to me, and I will do anything not to put a patient on insulin. I'll spend hours with them dealing with weight loss counseling before I'll consider insulin as an agent.

Susan Feeney:

Let's look at patients who are already on sulfonylureas, we have many, many people. Should we be switching those folks now to another agent based on this information?

Dr. Domino:

Well, I actually think if you can overcome the financial limitations of the newer agents, I think it's not an unreasonable thing at all to do. Think about it, patients with type 2 diabetes normally have multiple comorbidities, including risks for cardiovascular disease. So we've got a drug you're giving them that actually increases the risk of adverse cardiac events and cardiovascular events, including stroke, MI, and death. And those are pretty big adverse outcomes. So I think

there remains good data that we consider switching them off. I don't think there's any data that explains to us how. Sulfonylureas often have a fairly long half-life, at least 12 hours, so maybe stopping it for 24 to 48 to 72 hours, and then gradually adding the other agent in is a reasonable thing to do. Explain to the patients that these drugs have a different set of adverse risks and side effects, but that their risks are side effects are considerably less. And then provide close follow-up after you make the change.

The groups I worry about the greatest are my seniors. So here's a population again... I can think of one patient now who's in her early 90s, who's been on a sulfonylurea for the 21 years I've known her. And, A, she's change averse to begin with and now I'm gonna try to get her to change to a medication that may make her urinate more in an SGLT-2 inhibitor, she may not be too excited about that. So we have to use a good clinical judgment, but I think, in short, yeah, probably we need to slowly move our patients on sulfonylureas on to a different class of drug.

Susan Feeney:

Okay. What are the treatment goals for this particular patient, Marty, and how do we explain it to him?

Dr. Domino:

Okay. Well, as I said a little bit earlier, I think my treatment goal for him is to see what we can do to help his lifestyle and put him on an agent that's gonna help him succeed and not be counterproductive. So, for him in particular, I would certainly choose an SGLT-2 inhibitor, and I'd say, "Look, I can get your numbers down, but our real goal should be a 5% weight loss and getting you a little bit of exercise." So I'd ask him to choose one or the other that he wants to work on, weight loss or exercise, and then focus on that for the next two to three visits. Once we found his motivation and helped him along with that, I'd bring up the other. Weight loss would be an easy one 'cause if you put him on an SGLT-2 inhibitor, I think he's gonna probably lose a little bit of weight, and so now is a good time to have him make a dietary change, just one or two changes, and have him get that success of weight loss.

Following up every month or two, and once that's going well, talk to him about how he might change his behavior with regards to his work. Taking a five-minute walk every two hours, getting up from his computer, setting a timer, and getting him moving, have him find a buddy to exercise with, have him identify the piece of exercise furniture in his home that's covered by laundry and consider its use in his daily routine, help him identify what time of day is best for him to try to integrate it. And certainly journal those changes. So if he can keep track of whatever dietary changes he'd make and the days he exercises on and brings that in to show me, I feel very comfortable that I can probably help him live longer and better with his type 2 diabetes.

Susan Feeney:

And I really like that idea, is that you also give him a couple of things to work on and small goals, that you're not hitting him like, "You need to lose 60 pounds." You give him small goals that are not overwhelming, and along with the new med that will help with weight loss as well, so it's a great idea.

Dr. Domino:

Yeah. I always give patients like this I'll give them one month followups, and I'll just say, "Look, we're gonna have to see each other once a month for the next three to six months," and each time, at the end of the visit, I ask them to choose a goal and just focus on that for that month. People need that small bit of encouragement. They're overwhelmed when they think about the broad spectrum of the things that we tend to sometimes outline for them, so give them short, obtainable goals and help them to succeed.

Susan Feeney:

Great.

Dr. Domino:

Susan, thanks so much for joining me on this discussion.

Susan Feeney:

My pleasure.

Dr. Domino:

Practice pointer, sulfonylureas while valuable for the last 50 or 60 years, probably should become less and less a part of our practice, as they increase adverse risks, including cardiovascular outcomes and all-cause mortality. Join us next time when we'll be discussing the management of acute stroke in the office, in particular around the use of supplemental oxygen.