

Do We Still Use Warfarin? - Frankly Speaking EP 58

Transcript Details

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Dr. Frank Domino:

My Uncle George is an 88-year-old male and he's had AFib for quite a while. This has been well controlled with his medications, and he's been using warfarin to help prevent thromboembolic disease. Recently, his cardiologist told him he wanted to switch to a new drug, a direct-acting oral anticoagulant, and Uncle George is change-resistant. He calls and asks me what do I think he should do. Joining me on today's program to discuss this is Robert Baldor. Dr. Baldor is senior vice chair in the Department of Family Medicine and Community Health at the University of Massachusetts Medical School. Welcome to the show, Bob.

Robert A. Baldor, MD, FAAFP:

Thanks, Frank, glad to be here again.

Dr. Frank Domino:

Direct-acting oral anticoagulants, they seem to be quite a bit of literature about them. They're on the news, they're on advertisements day and night. Can you tell me a little bit about them so I can help interpret these things for my Uncle George?

Robert A. Baldor, MD, FAAFP:

Yeah. DOACs, as I'd like to call them, D-O-A-C is the way they're abbreviated, is just really interesting. You think about this, we're talking about medications to interfere with blood clotting. You have atrial fibrillation, you're a high-risk for blood clots with thromboembolic

disease to the brain and creating a stroke, that's the setting why we wanna treat people. For years, we've used warfarin. What is warfarin? It's a vitamin K antagonist. What the heck does that have to do with clotting? I wanna just take a minute talking about this so you understand what these newer agents are about. I wanna take you back to medical school. Remember the clotting cascade? There was a whole bunch of factors that ended up coming down to the cascade.

And then you had something called prothrombin, which was converted by factor X into thrombin. Thrombin then would kick off and have fibrinogen be converted into fibrin, and fibrin is what makes the clot. You wanna try and interfere somewhere along that line to prevent the clot from forming. Vitamin K is a cofactor for a number of these proteins involved in the clotting cascade. And, of course, one of the factors is it's factor II, which is prothrombin, or factor X which is the converting from prothrombin to thrombin. So, as people looked at this, they're saying, "Well, are there other agents we can use?" And Vitamin K has a whole bunch of factors. They came out more with some direct inhibitors. One class is the direct factor X inhibitors, there's factor Xa inhibitors that they have, and these are the classes where... And again, this is the agent that causes prothrombin to get converted into thrombin, as part of that. I have a lot of trouble saying these names, but it's apixaban, rivaroxaban, edoxaban, betrixaban, right now there's four agents.

Now, while we have agents to reverse warfarin bleeding using fresh frozen plasma, we don't have reversal agents for these, although there is one that's been out there, Andexanet, but FDA has not approved its use. And so the direct thrombin inhibitor actually does have a reversal agent, and that's called Daxaban. And again, these names are difficult to know, but that's the one agent that does have an FDA-approved reversal agent. Those are the agents out there. That's why they're called direct-acting is because they directly really act on the thrombin at that level and not on a whole bunch of different factors, like warfarin does.

The concern then has been around the efficacy of these agents, and a number of studies have shown they're just as efficacious. They work just as well, maybe even a little better in some studies than warfarin in preventing stroke in somebody with atrial fibrillation, and the concern

has been around the bleeding because... Particularly when we don't have reversal agents for these things. And most of these studies now have shown that the bleeding risk is actually okay, maybe even a little lower than with warfarin. The trouble is you look at most of these studies, they're saying, if you compare it to well-controlled warfarin, which means looking at the INRs in well-motivated patient is just as good, but if you go back and forth, some patients has to get around the warfarin either.

Dr. Frank Domino:

There's a recent study that just came out here, it was a meta-analysis and a cost-effective analysis that was done. It was just published here in the British Medical Journal, saying basically which is more effective for stroke prevention. Basically they looked at... I'm not gonna go into all the details, but they looked at efficacy, safety and cost-effectiveness of these direct-acting agents, compared to warfarin, from 23 randomized trials that had over 94,000 patients with atrial fibrillation. I'll just jump to the conclusions. What they concluded out of here was that these agents are really just as effective and safe, perhaps even safer, than warfarin. And then within the agents, they actually came up and they said, "You know what? Apixaban, administered twice daily, 5 milligrams twice daily, might be the most effective and safest alternative to warfarin for the prevention of stroke among patients with atrial fibrillation.

Wow, that's wonderful. We have meta-analysis based data that can help us figure some of this out. To recap, we've been using warfarin forever to try to decrease the risk of clot formation. We now have a variety of direct factor Xa inhibitors, but they can't be reversed. Whereas we have another class of DOACs that can be reversed, if necessary. And, in fact, they turn out to be as efficacious, if not maybe slightly more efficacious, than warfarin. Does that sound about right?

Robert A. Baldor, MD, FAAFP:

I would probably say they're non-inferior, non-inferior. But here's the story, it turns out, unlike warfarin, these have very short half-lives. We just stop the agent. We just stop the agent. And again, if you look at the safety profile on these things, it's about the same as warfarin. I certainly see that these are agents that have incredible use. It's hard to say this is the one to use versus the

others, because there's a lot of factors that go into whether it's patient choice. Also the cost factor plays in. These are a lot more expensive. Even if you add in some of the testing for warfarin, they're still more expensive. Some people can do at-home testing for warfarin, and so on.

Warfarin is still safe and efficacious, if done in the right environment. I have patients coming in that love these agents 'cause they don't have to think about their diet as much as they did with the warfarin. They don't have to think about the testing, and they just take this pill. But will their insurance cover it? What's on their formulary? So, it's an individual decision. The data's out there now saying these agents are effective and safe as, and maybe even a little better than warfarin. I'm feeling much more comfortable about using them, and I'm going to move more in that direction.

Dr. Frank Domino:

It certainly sounds like, when we're helping patients make this decision, we can feel reassured that the newer agents are as efficacious as warfarin. And it sounds like the big decision factors are not whether they're reversible or not, but rather are they gonna be cost effective for that individual patient, or are they able to afford that greater cost and, in return, get a much less confusing life with regards to diet and testing? Sound about right?

Robert A. Baldor, MD, FAAFP:

Sounds about right. I think we're gonna see more and more of those decisions coming up as we look at newer medications coming out. They're probably gonna be better and just as safe as things we're using. But the cost factor is gonna continue to be something we have to factor into those decisions.

Dr. Frank Domino:

Bob, thanks so much for bringing this concept forward. I think we're seeing more and more of these agents in our clinical care, and it's certainly reassuring to hear that they are safe and that they're equally efficacious.

Robert A. Baldor, MD, FAAFP:

Absolutely.

Dr. Frank Domino:

Practice pointer: Direct-acting oral anticoagulants are as effective as warfarin in the management of atrial fibrillation, and are likely just as safe. Join us next week when we talk about exercise as an intervention that has significant benefit for patients for primary prevention of cardiovascular disease.