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Aspirin Resistance and Its Implications in Clinical Practice

ASPIRIN RESISTANCE

Is your aspirin therapy working?

Welcome to the Clinician's Roundtable on ReachMD XM160, The Channel for Medical Professionals. I am Dr. Larry Kaskel, your host and I was recently at the Aspirin High-Tech Prevention summit and had a chance to sit down with Dr. Wayne Peters, who is the Medical Director of HealthMark and Assistant Clinical Professor of Medicine And Preventive Medicine and Biometrics at the University of Colorado School of Medicine and we talked a little bit about what aspirin resistance is and how to test it.

DR. LARRY KASKEL:

Dr. Peters, welcome to the Clinician's Roundtable.

DR. WAYNE PETERS:

Thank you very much.

DR. LARRY KASKEL:

Let's start with a little bit of history on aspirin, how long it's been around, who started it, and how it has changed over the last 100 years?

DR. WAYNE PETERS:

Well aspirin was actually identified or code invented back in 1900. It is a product of Germany and it was first available or marketed in the early 1900s in the United States. Well aspirin has gone through many, many decades of use and more recently many decades of sort of scientific examination and I think it's safe to say that most Americans now and certainly most of the medical community realize that aspirin has some definite values in the prevention of cardiovascular events at least in intermediate and high-risk patients.

DR. LARRY KASKEL:

Let's talk a little about the pathway and really where aspirin exerts its primary effect.

DR. WAYNE PETERS:

Well since most vascular events, heart attacks and strokes, are caused by blood clots. The whole idea has been how can we lessen someone's risk of having a blood clot, they don't need. We do need blood clots if we cut ourselves or have injuries, but the most part, many of us particularly have blockages in our arteries or diseased arteries have unnecessary clots. So, aspirin works on the platelet, which is responsible for the clotting of blood and it reduces the ability of that platelet to form a clot, if you really don't need one.

DR. LARRY KASKEL:

All right, so let's get into aspirin resistance. How common is it and what are the consequences thereof?

DR. WAYNE PETERS:

Since we recommend aspirin to people who are intermediate or high risk of having heart attacks or strokes either because they've already had one or because their cholesterol or blood pressure or either they have diabetes. People have looked at the whole concept does one size fit all when it comes to aspirin, and as they started looking at it through a variety of blood tests or more recently a urine test, they realized that somewhere between 5 to 40% of the population is resistant to at least the low doses of aspirin and a variety of reasons are present as to why that might occur. It has raised the whole spectra then. If we are truly trying to prevent a heart attack or stroke, may be we need to look and see, who might be aspirin resistant and who isn't to maximize our prevention efforts.

DR. LARRY KASKEL:

So, that's a pretty big numbers. So, potentially we are giving our patients aspirin and thinking everything is fine and they subsequently go on and have an event and we never even thought of checking to see if the medicine we are giving them is actually doing something. So, in primary care, what can I do to confirm that my patient is getting the benefit of the aspirin and it is actually working?

DR. WAYNE PETERS:

I think the easiest thing in primary care is to order an aspirin resistance test from the urine because all that patient has to do is submit a sample in a cup, which is given to the laboratory, it is sent off for an analysis and you get a quick reading on is the aspirin adequately suppressing the platelet function in this patient. Now there are other kinds of test that you can do where you draw blood and has to be in a very orderly fashion and then send it to the laboratory. The problem with that is nobody really likes to get their blood drawn if they don't really have to and so with the simplicity of the urine test, I can really tell someone with reassurance on whether the current dose of aspirin you are taking is being sufficient to lessen their platelet function and lessen their risk of blood clot.

DR. LARRY KASKEL:

Wayne, what screws up aspirin absorption or what messes with it's working well?

DR. WAYNE PETERS:

Well one of the most common things that happens when someone takes anti-inflammatory medications for arthritis or headaches or whatever sort of pain, more particularly ibuprofen, which is Motrin or Advil or other common brands is that type of medication can compete with the aspirin on the platelet and interfere with its benefit on reducing blood clot risk. So, if someone is going to take ibuprofen and aspirin, they need to take the aspirin first thing in the morning, wait 30 to 45 minutes, then take the ibuprofen through the rest of the day as directed, but they need to give the aspirin a chance to do its things before they potentially interfere with that effect by taking ibuprofen.

DR. LARRY KASKEL:

And besides the other nonsteroidals what else can create aspirin resistance?

DR. WAYNE PETERS:

Well just having high cholesterol, high LDL-cholesterol in and of itself can do that, can interfere with the benefits of aspirin and it may have to do with reasons why that person has a high cholesterol in the first place, some of those are genetic, many of them are lifestyle. Smoking cigarettes can interfere with the effectiveness of aspirin as well as can certain types of medication. Now lot of this is very preliminary and we don't have precise data and exactly, which medications and how much might interfere for sure we know about the ibuprofen, smoking, and if you do have a high cholesterol even more important to check for aspirin resistance.

DR. LARRY KASKEL:

If you have just tuned in, you are listening to the Clinician's Roundtable on ReachMD XM 160, The Channel for Medical Professionals. I am Dr. Larry Kaskel, your host, and I was recently at the Aspirin High-Tech Prevention summit and got to talk with Dr. Wayne Peters, who is the Medical Director of HealthMark and we were talking a little bit about aspirin resistance.

Wayne can you talk a little bit about some clinical trials that have been done that actually look at how urinary thromboxane may actually predict events like MI, stroke, or death.

DR. WAYNE PETERS:

The whole trial was a very large trial. Thousands of patients they were looking at a variety of things including using certain types of blood pressure medications and ACE inhibitors to lessen risk of vascular events. They did a subset of the whole trial where they actually looked at the urinary levels of thromboxane, which is what we test for to see if you are aspirin resistant and it turns out that those people, who had the least inhibition of thromboxane B2, which is in the clotting cascade, had the highest risk for MI, stroke, or death from cardiovascular events. It was increased 2-fold over the people who had the greatest response to the aspirin and a 2-fold increase in risk is not insignificant. Many of the risk factors we look for like high blood pressure, high cholesterol, smoking, etc., are in the 2 to 4-fold increase risk range.

DR. LARRY KASKEL:

Dr. Peters, when we look at high-risk patients, what do we do with dosing? Do we give him all the same dose to start with, do we give him a higher dose? How do we going to make that decision?

DR. WAYNE PETERS:

This is recently emerged into a very interesting discussion. For a long time it was stated that if you take a baby aspirin, which is 81 mg in this country that, that would probably suffice for most people. What we now realize is that 81 mg while it works in significant percent of population, simply isn't enough for many people because of this whole aspirin resistance story and so is there an ideal dose of aspirin that we could just say, lets give this to everybody and not worry about it, some people say well 2 baby aspirin, which is 162 mg or half of the regular aspirin tablet might be the ideal dose, but I think in a person, who has already had a cardiovascular event or in a person, who is at high-risk for one, but hasn't had the heart attack or stroke yet, then we really need to start with 81 and then check them a couple weeks later and see if in fact we have suppressed their platelet function to a significant degree or whether we need to then gradually move up the dose range to appropriately make sure that the aspirin is doing the job that it is supposed to do. Another thing that can affect absorption is the whole process of enterically coating the aspirin, therefore having less potential to cause GI side effects because if someone is going to have a major effect from aspirin, it is in their intestinal tract and occasionally people get bleeding from their stomach, which rarely can be life-threatening and so I think being thoughtful about how much you need and only using as much as you need is the important way to go here and that if it is an enteric-coated preparation, which may be easier on the stomach along with taking the aspirin at the time of a meal, then again we can gradually titrate the dose up, use the exact dose if they need for the prevention and hopefully minimize the risk of having any problems with bleeding in the stomach.

DR. LARRY KASKEL:

Wayne, tell me a little bit about the test what it's called, how we go about ordering it in our patients?

DR. WAYNE PETERS:

Well, this urinary test has got an easy name for it. It is called AspirinWorks and it's through a company called Corgenix. It should be available at your local laboratory either lab core or quest. All the doctor would really need to do is ask the person, who is drawing the blood or getting the urine specimen to order an AspirinWorks that company provides small plastic tubes that the urine needs to be put into transmit to the laboratory and then it is coated for prevention of vascular events and usually it's my experience that we've not had any difficulty in having it reimbursed. So, the key thing here is if the lab that the physician isn't really familiar with the AspirinWorks test, just to make sure that a representative has dropped off to the draw station or the doctor’s office the tubes that have AspirinWorks label on them so that it will preserve the urine in such a way that it can be analyzed and give a correct answer.

DR. LARRY KASKEL:

We talk a lot about the risk reduction of taking an aspirin being about 33%. We also hear the risk reduction of taking the statin is about 33% and it seems that everyone's on a statin and an aspirin, but yet we are not getting a 66% reduction. Can you comment on that?

DR. WAYNE PETERS:

Well your question really has to do with what's called residual risk. It is that no matter what sort of therapy we have used, it almost

always reduces the risk of a heart attack or stroke or cardiovascular death by about 33% and what that has made us realize is that he don't just give somebody a statin cholesterol medicine and say you are fine, your LDL cholesterol is under 70, you have no more risk for heart disease. What we have to do is a thoughtful combined approach. They need to be on a statin. They need to be on aspirin for sure, probably some fish oil. They need to have their blood pressure well controlled. They need to have their HDL cholesterol at least 45 or 50 in a man and 55 or 60 in a woman. They probably need to have their triglycerides lower. They need to lose weight. They need to quit smoking and you put all of those things together and may be some day we really can reduce the risk of having heart attack by 80% to 90% and so it's a combination effort not just take this pill and you will be free. So, I think Tim Russert was a classic example of that. He was taking a statin medication. His LDL cholesterol was under 70. People thought well may be he is at lower risk, but many of the other things were probably still present and may be not maximally treated and so it's a combination approach not just a single-issue approach for this.

DR. LARRY KASKEL:

Dr. Wayne Peters, thank you very much for talking with me today.

DR. WAYNE PETERS:

Thank you very much.

DR. LARRY KASKEL:

I am Dr. Larry Kaskel and you have been listening to the Clinician's Roundtable on ReachMD XM 160, The Channel for Medical Professionals. Please visit our website at reachmd.com, which now features our entire library through on-demand podcasts. You can also reach us by phone with comments or suggestions at (888 MD-XM160) and thanks for listening.