Polyposis: Are Orphan Drugs the Answer?

Researchers at Children's Mercy Kansas City are using a multi-pronged research approach to investigate the underlying causes of inherited conditions and possible new treatment options.

Dr. Seth Septer and partners are looking into the genotype and phenotype correlations within inherited gastrointestinal syndromes, such as familial adenomatous polyposis, to determine if patients may be at risk for certain type of cancer or a more aggressive form of cancer, depending on their gene mutations.

The team has already found success testing orphan drugs against patients tumor cells grown in a dish.

Dr. Seth Septer is here to discuss how he and his partners are making advances in hereditary polyposis and other inherited gastrointestinal conditions.

Featured Speaker:

Seth Septer, DO

Seth Septer, DO, is a pediatric gastroenterologist and the Director of the Polyposis Program at Children's Mercy Kansas City. Dr. Septer specializes in hereditary cancer and polyposis syndromes.

Learn more about Seth Septer, DO (https://www.childrensmercy.org/Clinics_and_Services/Clinics_and_Departments doc=11069)

Transcription:

Dr. Michael Smith: Welcome to *Transformational Pediatrics.* I'm Dr. Michael Smith, and our topic is "Polyposis: Are Orphan Drugs the Answer?" My guest is Dr. Seth Septer. Dr. Septer is a paediatric gastroenterologist and the director of the polyposis program at Children's Mercy - Kansas City. Dr. Septer welcome to the show.

Dr. Seth Septer: Hello. Yes, thanks for having me.

Dr. Michael Smith: So, how big of a problem is hereditary polyposis and other inherited gastrointestinal conditions?

Dr. Seth Septer: Well, these are fairly rare conditions when you look at them individually. So, we take care of patients with familial adenomatous polyposis or FAP, probably the most common syndrome. Some of the other conditions that we see in our clinic are Peutz-Jeghers Syndrome, juvenile polyposis, PTEN Hemartoma Syndrome, and so, each of those individually is fairly rare. FAP is seen in probably about one in 8,000 – 10,000 individuals, but that's not that rare. There are a large number of kids that we take care of in our clinic here in Kansas City with FAP and so, it's something that every couple of weeks we have a new patient diagnosed with this condition, it seems like. So, it's rare but not that rare is how I would put it.

Dr. Smith: And what's the standard treatment approach for hereditary polyposis?

Dr. Septer: Yes, so kind of going back to the FAP, one of the unfortunate things about it, if left alone, it's got basically a 100% lifetime risk of colon cancer and so to combat that, really the only effective treatment at this point is colectomy or surgery to remove the colon which is great because it pretty much eliminates the risk of colon cancer but it still leave those patients with a smaller, but continued, risk for cancer of the small intestine, sometimes cancer of the rectum and so colectomy is standard of care but it's still not the perfect cure, unfortunately.

Dr. Smith: And so how is--because I know this is kind of the work that you're focusing on--how is genetic testing changing the way that we're understanding these conditions and even treating these inherited conditions?

Dr. Septer: Genetic testing has been available and improving over the last years or even couple of decades and, in regards to FAP, we know the gene that the mutation occurs on called the APC gene, and so a good percentage of the time, we're able to find that mutation and give a solid diagnosis to a patient and then subsequently test the rest of the family, if they're at risk. Also, a lot of people have done a lot of work trying to determine whether the specific gene mutation that a patient has will help us predict their course. So, what we call genotype/phenotype correlations, where we match the very specific gene mutation to specific risks that may be higher in that patient, and so that has helped us tailor our surveillance a little bit to each individual patient, do a little more personalized type of medicine, a little bit more of what to expect for them, based on their specific genetic mutation.

Dr. Smith: And so, Dr Septer, some of them might have an inherited polyposis syndrome that has very high chance of colon cancer as an adult, but knowing some of these mutations, we may be able to discover which mutations are associated with more aggressive cancers, less aggressive cancers, and that might then change how you're going to treat them today, correct?

Dr. Septer: Yes. So, there's certain mutation thought to be more aggressive and so they may need colectomy surgery earlier in life. There are mutations that seem to give a higher risk for some of the other cancers that we see: thyroid cancer, hepatoblastoma, which is a tumor of the liver, small intestinal cancer. So, a specific person with one of those mutations, you may watch the thyroid more closely or you may watch the small intestine even more closely than you would on a different patient with a different mutation.

Dr. Smith: How often Dr. Septer are we using genetic testing in these cases? I mean, is this something that's really just done at the larger medical centers? Where are we, I guess, in this whole new era of genetic testing when it comes to polyposis?

Dr. Septer: Yes. I think in today's day and age, anyone who's suspected or is that high risk to have one of these conditions should be tested. I think that's clear and they should be tested sometime in the paediatric age group. So, it's important to know what you're looking for to order the right test and be able to interpret it. Genetic counselling is incredibly important in these cases to make sure, again, that the gene testing is used in the appropriate way and that the results are interpreted correctly, and that the rest of the family, if they might be at risk, is then tested appropriately. So, I think it should be being done, really, anywhere. Again, what you need is a genetic counselor and a physician who are familiar with the testing and know what to order and how to interpret it.

Dr. Smith: Let's switch gears a little bit here. Tell me about some of the research you're doing now with the orphan drugs for these conditions.

Dr. Septer: That's one of the projects that I have been working on in collaboration with some other people, is with FAP, I mentioned the only real cure or the only real treatment is colectomy surgery. It would be great if we had a medication that would either slow down the growth of these polyps or, in a perfect world, prevent the development of cancer. To this point, that's not been developed. Now, there have been somewhat promising ideas. People have looked at using, aspirin; a medication called Celecoxib; even things like Omega-3 fatty acids. Those all have been or are being looked at in an effort to slow down polyp growth or stop cancer. Doesn't seem like any of those, unfortunately, are a long-term permanent fix. There may be some benefit to them. So, one of the things we're looking at is trying to find new, potential treatments. So, looking at orphan drugs or drugs that have been used in the past for all sorts of different reasons, a lot of them may not even be in use any more. These may have been antibiotics or medications used 50 years ago that have been kind of abandoned and looking at those sorts of drugs, again, has developed new treatments for other cancers and conditions. So, we're trying to look at that. We're also looking at natural compounds, not medications but natural products and compounds that, either alone or in conjunction with medications might do the same thing. We are hoping to find a medication or a natural compound that would slow the growth of these polyps and these cancers.

Dr. Smith: And where you are? Are you working on patients with this or are you in the labs dealing with this in a petri dish adding the orphan drug and seeing the kind of result you get. Where exactly are you in the research?

Dr. Septer: We're still in the lab. We have got some grant funding in place and so the projects are on-going using actual polyp or adenoma cells and the improvements in the technology for this have been amazing. There's the ability here at the Kansas University Medical Center, and some of the people I'm collaborating with, have the ability to test hundreds, even thousands, of drugs and compounds at once against these cells. So, basically, we are taking a shotgun approach looking at a lot of different medications and compounds and then, the ones that look promising we'll study further in animal models and, hopefully, clinical trials eventually.

Dr. Smith: Well, Dr. Septer, I want to thank you for the work that you're doing and I want to thank you for coming on the show. You're listening to *Transformational Paediatrics* with Children's Mercy - Kansas City. For more information, you can go to ChildrensMercy.org. I'm Dr. Michael Smith. Have a great day.