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When to Consider Liver Transplantation for Patients with Hepatitis C

Announcer:
You're listening to ReachMD, the channel for medical professionals. Welcome to Advances in Transplantation, produced in cooperation with Indiana University Health, covering current issues and practices in transplant medicine. IU Health. Discover the strength of a leading national transplant center.

Your host is Dr. Aaron Carroll, Associate Professor of Pediatrics, Director of The Center for Health Policy and Professionalism Research, and Associate Director of Children's Health Services Research at Indiana University School of Medicine.

Dr. Aaron Carroll:
For some patients with chronic hepatitis C, managing the condition with medication does not stop progression of liver disease. When should liver transplants be considered for these patients? Our guest is Dr. Paul Kwo, Medical Director of the Adult Liver Transplant Program at Indiana University Health.

Welcome, Dr. Kwo.

Dr. Paul Kwo:
Thank you. It is good to be here.

Dr. Aaron Carroll:
How prevalent is hepatitis C?

Dr. Paul Kwo:
So hepatitis C, in the United States, is the most common blood born infection and the epidemic occurred 20 to 30 years ago, prior to us even having a diagnostic test for it. If you look at The Center for Disease Control data, they suggest that there is somewhere between 3 to 4 million people infected. That's probably a reasonable estimate. Some have postulated that it's actually a bit higher than that due to some populations that were excluded when they did the CDC surveillance, but we can all, I think, safely assume that there are at least 3 million people infected with hepatitis C in the United States. Worldwide, it's about 170 million people who are infected with the hepatitis C virus, and that's quite a bit higher than other blood born infections that we commonly hear about, say chronic hepatitis B or HIV.

Dr. Aaron Carroll:
What usually happens to people after they're infected with hepatitis C?

Dr. Paul Kwo:
It's very interesting. So with hepatitis C, it's different than other types of infectious hepatitis. So if you have, for instance, acute hepatitis A or B, particularly when you acquire this as an adult, you usually have symptoms. You turn yellow, you feel poorly, and you know you're ill. In adults with hepatitis C, the acute infection, 3/4s of the time, is without symptoms. You don't feel anything. And that's why there's a large pool of individuals who have chronic hepatitis C who don't know they have it because they acquired the disease, but without symptoms, they never thought to seek medical attention, and this disease can go undiagnosed, untreated for decades, until we get significant scarring of the liver and then it's the liver disease that produces symptoms, decades later, that causes somebody to seek medical attention.

Dr. Aaron Carroll:
So you keep discussing acute and also chronic hepatitis C. What's the difference between those two things and which one is more

common?

Dr. Paul Kwo:
Yes, so chronic hepatitis C is far more common and we have already been discussing that there are some 3 million people, at least, in the United States who are infected with the hepatitis C virus, and they're infected chronically. That is they typically have had it for years and most commonly, decades. Acute hepatitis C occurs when you get the virus at the initial infection and the most common risk factor in the United States is intravenous drug use and 20 to 30 years ago, when intravenous drug use was more common and it was not recognized that this was a risk factor for viral infections such as hepatitis C, this was the primary risk factor. It isn't the only risk factor. Any contact with infected blood can do it and indeed, something as snorting cocaine, blood transfusions, certain types of tattoos…there are a variety of ways that you can acquire acute hepatitis C, but again, as we discussed, only about a quarter or 25 percent have symptoms.

So that means 75 percent of people with acute hepatitis C, that means there is no…the liver is normal. You get infected. 75 percent of those people don't have symptoms. When you get acute hepatitis C, it doesn't go away about 85 percent of the time. So if you're infected with acute hepatitis C, 85 percent of the time, you're likely to go on to chronic hepatitis C. Fifteen percent of people actually get rid of it. That's different than some of the hepatitis viruses that we talk about. Hepatitis A, which we get through contaminated food, and essentially 100 percent of people get rid of it. Hepatitis B, if you're an adult and get hepatitis B, 90 percent of the time, you'll get rid of it. So hepatitis C is the opposite. When you're infected, you get the acute hepatitis, primarily without symptoms, and unfortunately, it does not go away 85 percent of the time.

Dr. Aaron Carroll:
What are the treatment options for people that get hepatitis C?

Dr. Paul Kwo:
So, the treatment options right now are primarily pegylated interferon and ribavirin. And the important thing people need to know about the treatment options for hepatitis C is that you can cure hepatitis C. That's unlike a lot of other chronic illnesses, but hepatitis, you can cure.

There are different species of hepatitis C, or what we call genotypes, and the most difficult and most common genotype in the United States is genotype 1. The cure rate right now for genotype 1 hepatitis C is about 40 percent, and then there are easier to treat species or genotypes of hepatitis C, genotypes 2 and 3, and your physician can easily tell you which of those you have, and the cure rate there are upwards of 80 percent.

Now these therapies are not short therapies. You have to be treated for anywhere from 6 to 12 months, and they are associated with some side effects, but the important thing to know, is that you can be treated successfully.

This summer we should see the approval of new agents which will improve the cure rates markedly, so for the genotype 1 infected individuals, who are the hardest to treat, so as I said, we should be seeing cure rates this summer with these new medicines, added to pegylated interferon and ribavirin, of somewhere between 70-75 percent.

And the important thing also, is the addition of these new medicine, will hopefully shorten the duration of therapy for many people who are infected with hepatitis C, such that we're hoping that around half of these individuals will be able to be treated for a shorter duration, say 6 months rather than a year.

Dr. Aaron Carroll:
Are these new medicines the NS3 protease inhibitors?

Dr. Paul Kwo:
Yes, they are. So they're what we call designer molecules. So interferon is a molecule that your body makes. So if you get the flu and you feel poorly, you have aches, you get a fever, that's your body releasing interferon to help the viral infection. And indeed, when you give interferon by injection, your providing additional stimulus for your body's immune system to help get rid of the virus. The ribavirin inhibits the hepatitis C but it is not a designer molecule. It works against a variety of viruses.

The protease inhibitors that you discussed are what we call designer molecules. They specifically attack one of the main proteins involved in hepatitis C replication, and it's the first of a future wave of therapies that we're going to be seeing that target specific areas of the hepatitis C replication, and the bonus is that they far more rapidly inhibit the hepatitis C replication and allow you to clear the virus very quickly, from the blood stream, and the NS3 protease inhibitors are the class that will likely be approved this summer.

Dr. Aaron Carroll:
If you're just joining us, you're listening to Advances in Transplantation on ReachMD, the channel for medical professionals. I'm your

host, Dr. Arron Carroll. Our guest is Dr. Paul Kwo, Medical Director of The Adult Liver Transplant Program at Indiana University Health. We're discussing when to consider liver transplants for patients with hepatitis C.

So for patients who go on to have chronic hepatitis C, how likely is it that they develop severe liver disease such as cirrhosis or even liver cancer?

Dr. Paul Kwo:
Yes, again, as we said, 85 percent of people don't get rid of the hepatitis C and the hepatitis C infects the liver, and over decades, causes scarring in the liver. And as a general rule of thumb, we say that 20 percent of people get cirrhosis with hepatitis C after 20 years. Now, that fibrosis progression can be more rapid. It's typically a bit slower and indeed, there are people who have been infected hepatitis C who have had it for 40 to 50 years and have minimum scarring. They peacefully exist with the hepatitis C, but in general, you could say that over 20, 30, 40 years, people progress from no scarring of the liver to fibrosis to cirrhosis, and it's these individuals that require consideration for liver transplantation. And indeed, in the United States, hepatitis C is the most common reason that people require liver transplantation.

Dr. Aaron Carroll:
When should liver transplant be considered for patients with hepatitis C?

Dr. Paul Kwo:
So you can live with cirrhosis for quite some period of time. Some people live and have a reasonable quality of life for 5 to 10 years, however when you get cirrhosis, you develop other complications. You typically can develop fatigue. When you develop hepatitis C related cirrhosis, you're at increased risk for liver cancer, and if you do have hepatitis C related cirrhosis, your doctor and you should discuss regular screening for liver cancer. But what we typically look at is whether or not the person is functioning well and whether or not the liver is functioning well. That is, that it's able to perform all of its functions, the bloodwork is relatively stable and you haven't developed any of the problems associated with cirrhosis when you decompensate. That is, the liver fails to perform its normal functions.

That means that the liver isn't developing ascites, which means fluid in the belly, your belly swells up, that you're not turning yellow or jaundice, that you're not confused, that you haven't developed liver cancer, and that you haven't developed any other problems like variceal bleeding where the pressure in the liver causes veins in the stomach and the esophagus, which are connected to the liver, and cause you to vomit up blood or what we call hematemesis or variceal bleeding. When you get those symptoms, that's called decompensation. The liver is not able to compensate anymore and at that time, you should at least start considering a liver transplant evaluation.

Dr. Aaron Carroll:
What is the evaluation process for liver transplantation?

Dr. Paul Kwo:
So when we see someone for liver transplantation, what we go on to do is, number one, make sure that they indeed have the evidence that the liver is not functioning well, and we want to make sure that also that the patient's quality of life is compromised by liver disease enough such that if we transplant them. That we're going to make them better. That is, some people come in with us for an evaluation, they may be working fulltime, and if they are, well, you know, if everything looks okay, you can just follow them. And we do see people like that. However, the vast majority of people with hepatitis C related cirrhosis and decompensation have a poor quality of life and the transplant evaluation is directed toward making sure that the patient can have the surgery safely. And what that means is that the heart and lungs are strong enough and indeed, you'll have lung testing, you'll have testing of your heart by a variety of methods to make sure that the heart will make it through the surgery. We'll make sure that the vessels that are attached to your liver are open, and we'll make sure that you have appropriate support. So that it's not only medical testing, but we want to make sure that someone has enough support to go through a transplant surgery, which for most people, will be likely the largest surgery that they will ever go through, and we want to make sure that patients are able to have the best chance of taking good care of their new liver that they will receive for the longest duration of time.

Dr. Aaron Carroll:
So what's the prognosis for a patient with hepatitis C after they've had a liver transplant?

Dr. Paul Kwo:
So what we do is we set…the most transplants in the United States are done for hepatitis C. Hepatitis C recurs 100 percent of the time. Essentially, once you get a transplant for hepatitis C, the new liver is, in general, infected all the time, and because of the immunosuppression that is given to help prevent rejection, it unfortunately makes the hepatitis C fibrosis rate much faster. So about 20 percent of individuals with hepatitis C, will develop cirrhosis after 20 years of infection, or two decades. When you've had a liver

transplant, that timeframe is accelerated dramatically and about 20 percent of people will have cirrhosis after just 5 years. So we try to keep a very close eye on these individuals and we try to intervene when appropriate to treat the hepatitis C. You can indeed cure hepatitis C post-transplant, but it's harder because of the immunosuppression makes it harder to get rid of the virus. I think that the upcoming newer agents that are going to be approved in the next several years will help allow us to, if you will, aggressively treat these people after a liver transplant, because with cirrhosis and hepatitis C, it's often very hard to treat people because they're very ill, they can tolerate the medicine.

Post-transplant, it's still a bit more difficult, but it's probably easier than it is when you're awaiting a liver transplant. And while we can treat approximately a third of people right now post-transplant who have hepatitis C, I think in a few years, the opportunity to successfully treat people and cure patients of their hepatitis C post-transplant will be much greater. But anyone who is having a liver transplant now should know that the expectation is that the fibrosis rate can be more rapid. It doesn't mean it always is, but can be more rapid after a liver transplant due to the immunosuppression.

Dr. Aaron Carroll:
Do people often need to be re-transplanted after they've had their initial transplant?

Dr. Paul Kwo:
Yes. So some people who cannot get rid of the virus do need to be re-transplanted, and again that sometimes can be a very difficult circumstance because we all do transplants for repeat hepatitis C, but that does make the circumstances more difficult because of the donor shortage.

Dr. Aaron Carroll:
We've been talking with Dr. Paul Kwo about when to consider liver transplants for patients with hepatitis C. Dr. Kwo, thank you, for being our guest.

Dr. Paul Kwo:
Thank you for having me.

Announcer:
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