Case Discussions

National HIV Curriculum Podcast

# Hepatitis C and HIV Coinfection: Diagnosis and Management

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National HIV Curriculum Podcast Editors Dr. Jehan Budak and Dr. Aley Kalapila discuss the diagnosis and management of hepatitis C co-infection in persons with HIV, including direct acting antiviral (DAA) therapy, use of the simplified treatment algorithm, and post-treatment follow-up.

Topics:

- OIs and HIV
- HCV
- DAA
- HBV
- hep C genotype

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Disclosures

**Disclosures for Jehan Z. Budak, MD**

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## Transcript

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introduction**[00:00] Introduction**

Hello, everyone. I'm Dr. Jehan Budak from the University of Washington in Seattle, and welcome to the National HIV Curriculum Podcast. This podcast is intended for health care professionals who are interested in learning more about the diagnosis, management, and prevention of HIV. I'm back with my colleague Aley Kalapila, an ID [infectious diseases] physician at Emory University in Atlanta. Hi, Aley.

Dr. Kalapila

Hi, Jehan. Hi, everyone. Excited to be back here again.

Dr. Budak

Today, we're going to talk about the management of hep C (or hepatitis C) coinfection in people with HIV, which is a scenario that we see quite often and clinically meaningful because we can cure hep C. First, I'd like to point out that Hepatitis C Online, the hep C curriculum, is an incredible resource, and I actually recommend watching Dr. Maria Corcorran's excellent mini-lectures on that site for details about hepatitis C treatment. With that in mind, today, through a conversation about a patient of Aley's, we'll discuss general principles of the evaluation and management of hepatitis C in a person with HIV.

hcv-screening**[01:05] HCV Screening**

So, Aley, let's dive right in with the case of a 27-year-old man with well-controlled HIV who comes in for routine primary care follow-up. At this visit, he has no concerns and endorses full adherence to his antiretroviral therapy (ART). You obtain routine labs and STI (or a sexually transmitted infection) screening and you also screened him for hepatitis C. So, what is your practice regarding hepatitis C screening?

Dr. Kalapila

So, the Health and Human Services (or HHS) guidelines typically recommend that anyone diagnosed with HIV should have routine screening for hepatitis C infection and entry into care. And also, anyone who remains at risk for hepatitis C acquisition should be screened annually, at least, for hepatitis C. Now, I think that everyone is aware that people can acquire hep C through percutaneous transmission, especially among people with injection drug use, but recent epidemiologic trends also show that there is an increasing hepatitis C incidence among younger individuals in the U.S. A lot of this, of course, not surprisingly driven by the opioid epidemic, but in addition to this, providers should also be aware that hep C *can* be sexually acquired. Now, typically, we see this among men who have sex with men and especially if there is concomitant stimulant substance use as well.

Dr. Budak

So, you mentioned screening at least annually for hepatitis C. Do you ever screen for hepatitis C more frequently than annually?

Dr. Kalapila

I check for hep C more often than the annual recommendation if the patient is symptomatic or had an asymptomatic transaminitis in their liver function tests, but I suppose that's technically diagnosis and not necessarily screening.

hcv-testing**[02:45] HCV Testing**

Dr. Budak

Okay. Back to your patient, routine labs on him showed a normal complete blood count (or CBC) and a normal comprehensive metabolic panel (or CMP). His HIV RNA was undetectable and STI testing was notable for rectal chlamydia, which you treated. His hepatitis C antibody was positive, and his last prior hepatitis C antibody test was negative approximately one year ago. So, first, can you talk a little bit about the testing modalities?

Dr. Kalapila

Sure. So, many point-of-care and lab-based hepatitis C screening tests only detect a hepatitis C antibody. A positive hepatitis C antibody test only confirms exposure to hepatitis C but does not actually indicate active infection. Now, active hep C infection is defined by a detectable hepatitis C RNA level (or hepatitis C viral load), which typically requires a separate test. Now, fortunately, in our lab, once we send off the hep C antibody test, if it is positive, the lab auto reflexively obtains a hepatitis C RNA.

Dr. Budak

Great. In our systems laboratory, I also can order the hep C antibody with a reflex PCR [polymerase chain reaction]. So, in your patient, he had the antibody, it reflexed to a PCR, and his hepatitis C viral load came back at 1.6 million international units per milliliter (1.6 million IU/mL).

Dr. Kalapila

Right. So this confirms that he has active hep C infection. The quantification of the viral load, the actual number, is much less relevant than the fact that he actually has a detectable hepatitis C viremia, and so, in this case, this person has active hep C infection and we should consider treating him for hepatitis C.

Dr. Budak

Now, about 15 to 20% of individuals who newly acquire hepatitis C will go on to spontaneously clear their hep C infection without any intervention. However, this rate is lower among people with HIV, so in his case, Aley, he has active hepatitis C but his liver function tests (or LFTs) are normal. What do you make of that?

Dr. Kalapila

That is actually a pretty common scenario, so unlike other viral hepatitdes, like hepatitis A or even hep B, patients with hep C may actually have very subtle changes in their LFTs, if at all. So, you're talking about elevations that may only be about one and a half times the upper limit of normal, and those two may normalize pretty quickly as a patient transitions from acute and maybe symptomatic infection to a more chronic and less symptomatic infection.

treat-acute-hcv**[05:13] Treat Acute HCV?**

Dr. Budak

Is it right that whereas previously, we used to wait for people to clear and not treat acute hepatitis C infection? Guidelines now recommend also treating acute hep C.

Dr. Kalapila

You're absolutely right. When we used to treat hepatitis C with interferon, which was a long time ago, certainly when I was in fellowship training, differentiating between acute and chronic hep C infection was much more important because of the differences in cure rates and because of toxicities associated with interferon treatment. Now, in the days of directly acting antiviral therapy (or what we call now DAAs), we have excellent cure rates for both acute and chronic hep C, and so the differentiation between these two, sort of, types of infection really doesn't matter. But early recognition of acute hep C in patients with newly elevated liver enzymes is pretty important because we have effective treatments. If we can start treatment sooner rather than later, then this will actually improve outcomes and maybe even prevent transmission as well.

pre-treatment-assessment**[06:20] Pre-Treatment Assessment**

Dr. Budak

So, all that to say, we can and should treat both acute hep C and chronic hep C. And, now that we've discussed testing and terminology, let's discuss the workup necessary prior to treatment.

Dr. Kalapila

So, assuming that the patient is interested in hepatitis C treatment, the first step is to determine whether or not the patient qualifies for the AASLD-IDSA simplified treatment algorithm for hepatitis C. AASLD is the American Association for the Study of Liver Diseases and IDSA is the Infectious Diseases Society of America, and both of these organizations have collaborated to come up with guidelines for treatment of hepatitis C and they have a simplified treatment algorithm.

Dr. Budak

My understanding is that the simplified treatment algorithm includes both the pre-treatment assessment and the treatment options themselves, both of which are streamlined with this algorithm.

Dr. Kalapila

Yes. The AASLD-IDSA recommend obtaining a few labs to determine the eligibility for the simplified treatment approach, and so these labs basically are the foundation for your pre-treatment assessment. So, these include a baseline CBC and CMP, a hepatitis B (as in boy) surface antigen, and an evaluation for cirrhosis. Now, whereas the gold standard to diagnose cirrhosis is a liver biopsy, we are now able to use noninvasive testing such as a FIB-4 score (or transient elastography or FibroScan) to help ascertain whether or not the patient has cirrhosis. Now, a FibroScan is like a special type of ultrasound, and the FIB-4 is a widely used index that we can calculate based on four factors that include the person's age; the AST [aspartate aminotransferase] and ALT [alanine aminotransferase] (these are liver function tests); and a platelet count. And, I usually use an online medical calculator to calculate the FIB-4 once I have the patient's CBC and CMP results available.

Now, both the FIB-4 and the FibroScan have a high negative predictive value for excluding advanced cirrhosis. I would also recommend when you're evaluating the patient to look at other factors that might imply that a patient has cirrhosis. Now, these can include things like say a patient has stigmata portal hypertension either on a physical exam or on imaging and they might have low platelets which is related to splenomegaly, which

is related to essentially stigmata portal hypertension, or they could have a high INR [international normalized ratio]. In all of these cases, I would be predisposed to considering them as having cirrhosis when determining my treatment plan. Now, in reality, most people will qualify for simplified treatment if they have a new diagnosis of hepatitis C, they do not have decompensated cirrhosis, and they do not have concomitant hepatitis B infection, and they're not pregnant.

hbv-flare**[09:20] HBV Flare**

Dr. Budak

This issue of concomitant hepatitis B infection is an interesting point. So, currently, the hepatitis C DAAs have a "black box" warning about the risk of hep B reactivation in individuals who have infection with both hepatitis B and hep C. So, while the exact mechanism is not entirely clear, this risk is believed to be due to a shift in the host's immune response and a reduced hepatic interferon response after their hep C is treated, which allows hep B virus to replicate more freely. As the hep C viral load comes down, endogenous interferon levels wane, and this can lead to the precipitation of a hep B reactivation or a flare.

Dr. Kalapila

Yes, that is exactly right. With our patients with HIV who happen to have hepatitis C *and* hepatitis B coinfection, this issue of having a hep B flare with hepatitis C treatment is less of a problem. And the reason for that is because their HIV antiretroviral therapy includes treatment for both HIV and hepatitis B. Now, if someone has hep C and hep B coinfection but does not have HIV, then they would need to be initiated on hepatitis B treatment at the same time as their hep C DAA treatment in order to avoid flare of their hep B infection.

ultrasound**[10:42] Ultrasound?**

Dr. Budak

So now, let's go back to the liver elastography or FibroScan. What if people don't have access to that? Should they get a right upper quadrant ultrasound?

Dr. Kalapila

You don't really need to do a right upper quadrant ultrasound to determine whether someone qualifies for simplified treatment. In fact, the guidelines really state that all you need to do is calculate a FIB-4 score. Now, if the FIB-4 score is greater than 3.25 or exam findings are concerning for cirrhosis, I usually will go ahead and get an right upper quadrant ultrasound, but I never delay treatment waiting for it. And the reason I actually get the right upper quadrant ultrasound is that the patient would need an ultrasound for HCC (or hepatocellular carcinoma) screening, which is part of their routine cirrhosis management. It doesn't necessarily pertain to their hepatitis C treatment. Cirrhosis management is a topic for a whole other discussion at another time.

hcv-genotype**[11:38] HCV Genotype**

Dr. Budak

And so, what about getting a hepatitis C genotype?

Dr. Kalapila

So, great question! Typically, you do not need a genotype to determine eligibility for simplified hepatitis C treatment, and this is written in the guidelines. The reason for this is because the medications that are

recommended for simplified hepatitis C treatment are pangenotypic or treat multiple genotypes. Now, this is, in the ideal world, the optimal approach, but the reality is often different in clinical practice, and the reason is because of insurance. So, I often will get a genotype at my baseline hepatitis C visit because, first of all, it's an easy test for me to obtain in my clinic, and also because I usually anticipate that the patient's insurer will have a preferred hepatitis C treatment option that may not necessarily be a pangenotypic option that is listed in the guidelines. So in order to avoid any delays in patient care, I preemptively obtain that genotype at the initial visit. But as I mentioned before, this is by no means necessary in order to kind of move the patient along on the simplified hepatitis C treatment approach.

Now, there is one clinical scenario where getting a genotype ahead of time is recommended by guidelines, and this is when a patient has compensated cirrhosis and is going to receive the drugs combinations sofosbuvir with velpatasvir.

Dr. Budak

That is such a useful practical pearl, and for the purposes of this talk, we'll focus on the hep C meds that are pangenotypic agents.

other-assessments**[13:21] Other Assessments?**

Before we talk about the treatment and the DAAs, is there anything else you'd like to mention?

Dr. Kalapila

Yes. I think that in the initial visits, when you are evaluating eligibility for simplified treatment, it is helpful to do some other health care maintenance. So, for instance, I will always check hepatitis A and hepatitis B serologies. I mean, we already have mentioned the fact that we are going to get their hepatitis B surface antigen, but I usually will do the full hep B surface antibody panel if I don't have it, which also includes a surface antibody and a hepatitis B core antibody, and then also check their hepatitis A serologies. And this is, first of all, recommended for all individuals with HIV at entry into care anyway, and if these individuals are not immunized against hepatitis A and hepatitis B, then I will also be recommending immunizations, because this is, again, part of routine HIV primary care. I also will use this as an opportunity to link my patients to other resources based on their risk factors for hepatitis C acquisition, such as medication assisted therapy for opioid use disorder for instance.

Now, if their risk factor is sexual transmission of hepatitis C, then I would consider recommending HIV PrEP (or preexposure prophylaxis) if they don't have HIV already. You can consider recommending doxy PEP if they meet criteria for that (or doxy post-exposure prophylaxis). This is really also a time to discuss other modifiable behaviors that may impact their overall liver health, right? So, this is the time when I would discuss alcohol use, obesity, et cetera. And then, you know, the last thing I always talk about with patients is that while I am confident that I will be able to successfully treat their hepatitis C infection, I do counsel them that curing hepatitis C does not confer immunity. What this means is that the patient continues to remain at risk for hepatitis C reacquisition even after successful hepatitis C treatment and cure. So, I always will advise my patients to try to modify their risk factors, whatever they might be, to prevent them from having to get hepatitis C infection again.

Dr. Budak

Okay, so we'll go back to your patient who ended up having a normal CBC, a normal creatinine, a slightly elevated AST and ALT, approximately 1.5 times the upper limit of normal, and a normal FIB-4 score. So, based on what you've said, he qualifies for simplified treatment. And, to reiterate for our listeners, most persons with hepatitis C are eligible for simplified treatment, as Aley had mentioned, regardless of genotype, if they do not have decompensated cirrhosis, and are treatment naïve, including persons with HIV.

daa-treatment-disqualifiers**[16:00] DAA Treatment Disqualifiers**

Dr. Budak

In addition, you're not eligible for use of the simplified algorithm if you have any of the following. A history of prior hepatitis C treatment, liver transplantation, a positive hepatitis B (as in boy) surface antigen, are currently pregnant, have known or suspected HCC (or hepatocellular) carcinoma, or have compensated cirrhosis but with end-stage renal disease. And so, I know that Aley has touched on many of those, but I just wanted to reiterate it again. And also, for persons with HIV, the other reason individuals may not qualify for simplified treatment is because of potential drug-drug interactions between their antiretroviral therapy and the hep C DAAs.

Dr. Kalapila

So, yes. People with HIV are not eligible for simplified hepatitis C algorithm if they are on ART regimen containing efavirenz, e-trav-ir-ine or et-ra-vi-rine (however you choose to pronounce it), nevirapine, or boosted HIV-I protease inhibitors. They're also not eligible for simplified hepatitis C algorithm if they are on an ART regimen that contains tenofovir disoproxil fumarate (or TDF) with an eGFR (or glomerular filtration rate) less than 60 mils per minute. Now, fortunately, this shouldn't be a frequent issue as most of our patients in the United States are on regimens containing integrase inhibitors and many receive tenofovir alafenamide (or TAF) rather than TDF.

g-p-or-sof-vel**[17:25] G-P or SOF-VEL?**

Dr. Budak

And so, luckily, your patient is on bictegravir, tenofovir alafenamide, and emtricitabine. So, it sounds like based on that and based on his pre-treatment labs, he qualifies for simplified treatment of his hep C infection, so what are his treatment options?

Dr. Kalapila

That's great! So, he has two hepatitis C DAAs (or direct-acting antivirals) that he's eligible for based on the simplified treatment algorithm. So, one option is glecaprevir-pibrentasvir and the other one is sofosbuvir-velpatasvir combination. Now, these are a mouthful, so I'm going to refer to the former as G-P and then the latter as SOF-VEL. Now, without getting too in the weeds, first of all, I think it is important to mention that both the drug combinations contain medications that act on two different parts of the hepatitis C life cycle. So, in many ways, this is quite similar to how we think about combination antiretroviral therapy for HIV infection. These hepatitis C medications have cure rates that are greater than 95%, including in people with HIV.

Dr. Budak

Sounds like you have two great options, one is G-P, one is SOF-VEL. How do you choose between the two?

Dr. Kalapila

So, both are equally recommended. Oftentimes, the regimen I choose depends on, first off, what their insurance is going to cover. If that isn't an issue, then the first thing I do is to ensure that there are no drug interactions between their other medications and their antiretroviral therapy, as well as the DAAs. Now, for this, I discuss with a pharmacist, and I also use the online University of Liverpool Hepatitis C Drug Interaction Checker, as well.

Dr. Budak

That University of Liverpool website is excellent, and, for our listeners, it's a free website and a great resource for all.

Dr. Kalapila

So, if there are no drug interactions with either G-P or SOF-VEL, then I will discuss with the patient as to what they prefer. Now, the G-P regimen entails taking three tablets once a day with food for eight weeks, whereas SOF-VEL is one tablet once a day for 12 weeks. So, in best-case scenario, if there's no drug interactions and there's no insurance requirement, then I'll ask the patient what they prefer. But oftentimes, I will tell you that, in clinical practice, the reality is usually determined by insurance coverage.

monitoring**[20:00] Monitoring**

Dr. Budak

So, your patient chose SOF-VEL. Once he starts, is any on-treatment lab monitoring needed and are you seeing him more frequently in clinic during this time?

Dr. Kalapila

The hepatitis C DAA regimens are very well tolerated, so once a patient has actually been initiated on their therapy, you do not need to see them until 12 weeks after they've completed treatment, which is remarkable and really speaks to the tolerability as well as the safety of these drugs and the efficacy of these drugs. Because, again, patients don't typically require on-treatment lab monitoring, you're only really going to have to see them 12 weeks after they complete treatment. Now, the guidelines recommend checking a hepatitis C RNA and a liver function panel 12 weeks after treatment is completed. This is often referred to as a sustained virologic response at 12 weeks, or we abbreviate it often as an SVR12, and this is considered the marker for cure.

Now, as with most aspects of patient care, this is definitely not a one-size-fits-all approach. I always counsel providers and let them know that they should tailor their treatment plan to optimize their patient's chance of cure. So, if there are barriers to care or adherence, such as housing insecurity or active substance use, then you should consider increasing the frequency of your visits with the patient, for example, or using telemedicine visits, if that is feasible, or doing whatever really is necessary to ensure that the patient is able to continue to take their antivirals and that you can allow them to move along successfully through the hepatitis C continuum of care.

Dr. Budak

Exactly, and along those lines, this is also an opportunity to use a multidisciplinary team-based approach to move the patient through the hep C continuum of care.

Dr. Kalapila

Absolutely. I think you and I both have robust pharmacy support, as well as nursing assistants, who often will connect with patients to ensure that they pick up their medications, take their medications, and complete their hep C treatment successfully.

post-treatment-follow-up**[22:05] Post-Treatment Follow-Up**

Dr. Budak

Your patient successfully completed therapy and achieved SVR12, what counseling do you do at the end of the treatment?

Dr. Kalapila

So, I obviously congratulate them first in successfully completing treatment and achieving hepatitis C cure, always such good news to give to a patient. Then I use it as an opportunity to once again discuss harm reduction strategies to mitigate their risk of hepatitis C reinfection.

Dr. Budak

What if someone isn't consistently taking their medications or there is concern for inadequate response to therapy, such as if their 12-week hep C viral load was still elevated?

Dr. Kalapila

In those instances, I will refer to the AASLD-IDSA hepatitis C treatment guidelines. They're quite thorough and there are recommendations in there for patients that have missed one week or more of medications and also what to do if treatment wasn't successful. And this is often a good time to involve someone who is a hepatitis C expert.

Dr. Budak

And what about follow-up screening for hepatitis C after having completed therapy?

Dr. Kalapila

So, after successful hep C DAA therapy, I do continue to screen the patient annually if they have ongoing risk factors for reacquisition of hep C. Now, since their Hep C antibody is always going to be positive, my re-screening is done by checking a hepatitis C RNA (or a hepatitis C viral load). If the patient has cirrhosis, then it is important to continue to perform every six months surveillance for hepatocellular carcinoma with a hepatic ultrasound and also a serum alpha-fetoprotein level as well.

Dr. Budak

Aley, what a great overview. Thank you so much, including taking us through some of these key principles of treatment.

summary-points**[23:45] Summary Points**

Dr. Budak

So, some summary points to wrap up. All persons with HIV should be screened for hep C at entry into care and annually for those at high risk for hepatitis C infection. The new hep C DAAs have very high cure rates, and most patients will qualify for the AASLD-IDSA's simplified treatment algorithm. And again, HIV does not exclude the patient from that algorithm. Since the new hepatitis C drugs are well tolerated, most patients don't need on-treatment lab monitoring, and a hep C RNA should be checked 12 weeks after treatment completion to determine response to therapy.

Aley, thank you so much. We'll see you next time.

Dr. Kalapila

Great, thank you. Bye.

credits**[24:23] Credits**

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