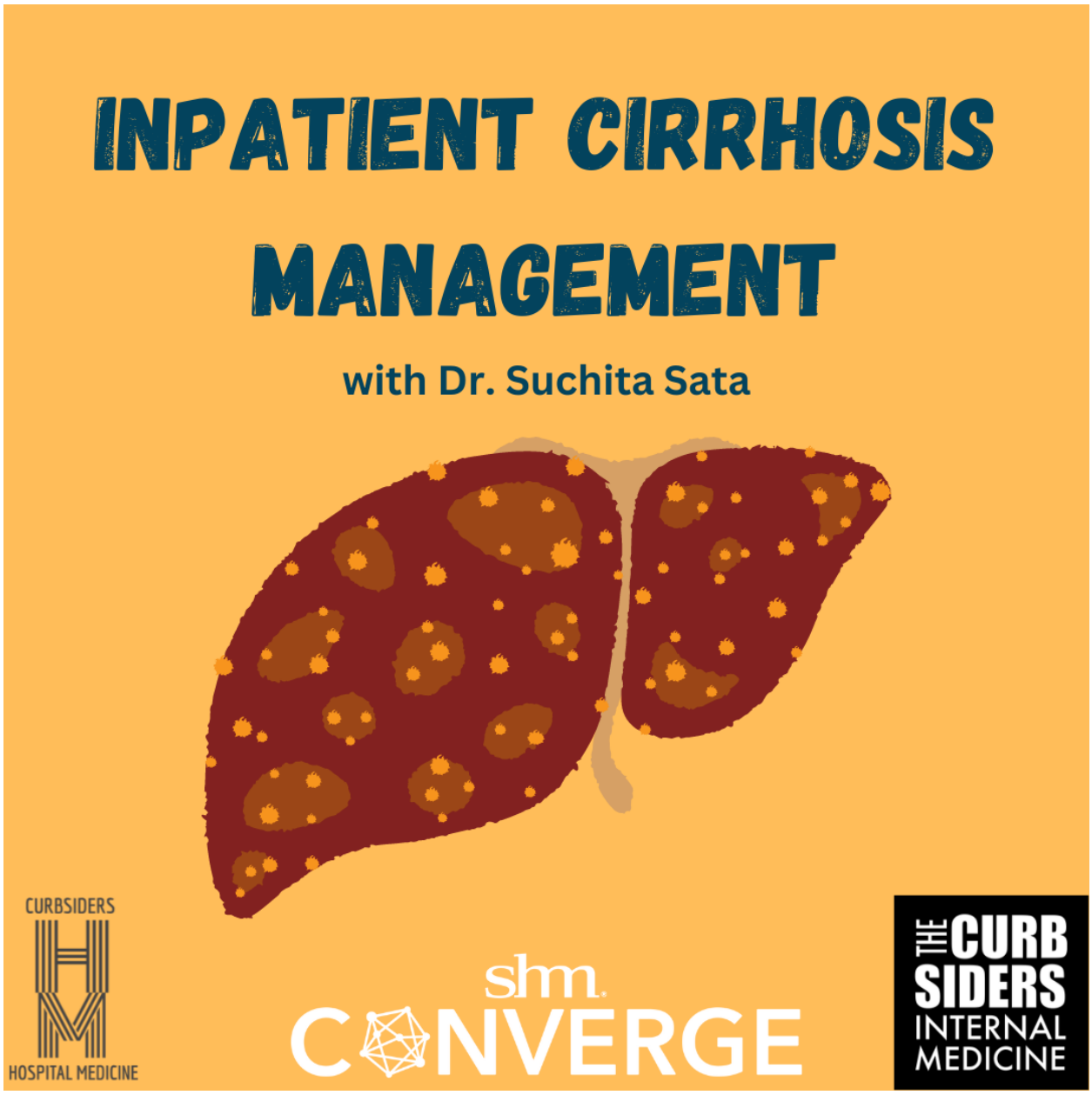
398:Live! From SHM: Inpatient Cirrhosis Management



Meredith: Hey Curbsiders, Meredith and Monee here. Just wanting to plug one more time that the Hospital Medicine episodes are going to come out on the first Monday of every month. So, tune in for more Hospital Medicine content. Again, 1st Monday of every month, because the first must mean it's better.

Monee: Yeah. Get excited, people.

[Disclaimer]

[The Curbsiders theme]

Monee: Hey Curbsiders, Monee, this is the last of our three episodes we did from SHM. It was recorded live, but obviously not live for you. This one is acute liver management with the wonderful Dr. Suchita Sata out of Duke. And we can't wait for you to hear this one. So here we go. And we're back live from Austin in a conference room. Meredith, good to see you again.

Meredith: You, too. With a little less echo this time.

Monee: A little bit or more? I don't know. We're actually really excited because we just got out of this fantastic talk by Dr. Suchita Sata from Duke about decompensated cirrhosis in the acute setting, and we're really excited to be able to basically go over her talk in this conversational form. So, before we do that, Dr. Sata, would you please tell us a little bit about yourself?

Suchita: Thanks so much, Monee and Meredith. I am riding the high. I've given a talk in a big ballroom. I am a 30-something-year-old woman in medicine, academic hospitalist at Duke University Hospital, first-time mom to a seven-month-old. I am an academic hospitalist and clinician educator, teaching and driving high-value care while simultaneously coaching and mentoring the next generation of academic hospitalists.

Meredith: Fabulous.

Monee: Fantastic.

Meredith: I think we'll stick to our Austin theme picks of the week. And since we're sort of on a time limit, I think we'll just keep it there. Monee, do you want to go first?

Monee: No, because I need to think of one and that's what you got?

[laughter]

Meredith: No, I think I'll just stick to your food theme because I know you're not going to be able to do this. And even though we haven't actually gone to do this yet, I'll say it. Texas Barbecue is the best, brisket the way to go. I know I'm talking to a vegetarian right now, but that's okay. But I'm just excited to be back in a state that knows how to do some good barbecue.

Monee: That must be wonderful. I am from Kansas City, which apparently has good barbecue as well. Not that I would know. My pick of the week is going to be sentimental. I got to meet

Meredith's parents, spend some time with them, which was super fun. And we had a really good meal, too, actually. It was called-- [crosstalk]

Meredith: Peacock, is the restaurant?

Monee: Yeah. Mediterranean food is delicious. Suchita do you have an Austin pick of the week for us?

Suchita: Well, I'm from North Carolina and Carolina barbecue is a thing, but we had the chance to go to Epoch Coffee, which is a local coffee shop, and have a delicious beverage. And my Austin pick of the week is going to be SHM Converge. Because I know it's a great city, but I am here for this awesome convention and Society of Hospital Medicine conference is the best conference out there. It's a great place to network and learn and just have a lot of fun with people all across the country.

Monee: Yeah. If you've been watching our social media feeds during the conference, you'll know that CEO Eric Howell agrees. So, now we're excited to be here, too. I think we should just jump in. Does that sound good?

Meredith: I like it. So, we have Mr. Murphy. He's a 56-year-old male and he presents with new-onset abdominal swelling. He hasn't seen a doctor in 10 years, and while he's hemodynamically stable on presentation, he does have fluid wave on exam and his notable labs include a white count of 6, creatinine of 1.1, and an INR of 1.9. So, we're talking a little bit about new-onset ascites and obviously some decompensated cirrhosis here. And I think the best place to start Suchita would be if you could walk us through some of the pathophysiology of decompensated cirrhosis.

Suchita: Yeah, I love talking about decompensated cirrhosis and I think that Mr. Murphy like you said has ascites on exam. So first, I guess, take a step back. What is decompensation in cirrhosis? And traditionally, it's defined as the onset of ascites or a variceal bleed, though we can think about it as any essentially organ dysfunction or complication related to chronic liver disease. So, people can live with cirrhosis without a symptom, but when they come in to see us as hospitalists, it's because they're ill, whether that's a presentation of ascites or worsening of ascites, and the discomfort that leads from that. The infection, spontaneous bacterial peritonitis, hepatorenal syndrome with acute kidney injury, GI bleeding, portosystemic encephalopathy, which is what everyone likes to call what I call hepatic encephalopathy now. And those are the main things we think about with decompensation.

So, how I approach the patient with newly decompensated cirrhosis is in a systematic way. I mentioned all those examples of decompensation, but they can all lead to each other and from each other. So, ascites can lead to hepatorenal syndrome. Hepatorenal syndrome can lead to encephalopathy. Encephalopathy could be due to SBP. SBP can also lead to hepatorenal syndrome. It's all just this giant circle of related physiology. And so, we take a step back to actually answer the question you asked me of what is physiology here. We have the liver, we have a circulation in the portal system. It's portal vein and then the splenic vein.

And we have a fibrotic liver with portal venous hypertension that leads to congestion in the gastroesophageal venous system and decreased blood flow peripherally. vasodilation peripherally, and that leads to decreased blood flow to the kidneys. So, renin-angiotensin-aldosterone upregulation, plasma renin activity is increased that leads to salt and water retention. So, you have fluid accumulation because of that. So, that leads to things like ascites and then future kidney injury.

Cirrhosis is also a problem of synthetic function of the liver. And we think about synthesis in terms of proteins as well as the clotting factors. And it's also a problem of clearance of the metabolites that leads to encephalopathy. So, we have coagulopathy because of the clotting factor synthesis problems, we have encephalopathy related to suboptimal clearance, and then we have all the fluid and hemodynamic issues related to the RAAS system with how the kidney's blood flow is impacted. So, as much as cirrhosis is a liver problem, the kidneys play a vital role into it also, the selfish, selfish organs need the blood flow.

Monee: Yeah, it's always a system and there're too many things leading to another and it's very hard to keep straight. I think a really good place to start in terms of what we're doing is ascites. And what do you do with especially this patient who came in with new-onset ascites? Where do you start when they walk in and you're working them up?

Suchita: You have to take a systematic approach for every patient who comes in with new-onset ascites. I mentioned that there're all these things that could be the triggers, and so we have to systematically evaluate it because most of those don't have symptoms with it. Ascites is the sign that is a harbinger of underlying issues. So, ascites doesn't develop completely by itself usually, right, it is often triggered by something in that person that has changed or gotten worse or progressed to the point of now having ascites.

So, you have to think about the portal venous system. Is there a portal vein thrombosis? Every patient who comes in by guidelines should have imaging to evaluate for portal venous thrombosis, whether that's a right upper quadrant ultrasound with Dopplers or a CT scan. And also, every single patient with new onset or worsening ascites or patients who are hospitalized with ascites should have a diagnostic paracentesis.

And that is per the AASLD guidelines. And we often think about we don't need to do a paracentesis in somebody because I don't clinically think they have an infection, right. We think about infection being CERS criteria, white count, fever, symptoms, abdominal pain. SBP is purely a cellular diagnosis or spontaneous bacterial peritonitis could only be diagnosed with a diagnostic paracentesis. So, if you're not looking, you're not going to find it. So, I think about the etiology of ascites first with what is driving this right now. So, in addition to a good history of what's the patient's intake, what triggers have they had recently, the imaging of assessing the portal vein and then the diagnosis with diagnostic paracentesis can help you identify the etiology of the ascites.

Meredith: So, going through that etiology, when you do find that portal vein thrombosis in someone, can you walk us through the treatment and the thought process for deciding on anticoagulation and all of that?

Suchita: Yeah. So first, if you are finding a portal vein thrombosis on ultrasound, confirming it on cross-sectional imaging is important. And then you have to ask yourself, "Should I anti-coagulate the portal vein thrombus in this person? And there is definitely a risk to anticoagulating a clot in someone with cirrhosis because there is coagulopathy associated. They're at high bleeding risk but also high clotting risk.

Is that portal vein thrombosis clinically significant enough to put somebody through the risk of treating them with therapeutic anticoagulation? So, as we ask ourselves that, I'm going to jump ahead to the answer of you can use heparin acutely in the hospital but transitioning them to low molecular-weight heparin. And we still use warfarin even though it's hard to monitor INR. And then there are some smaller studies that have looked at DOACs, particularly rivaroxaban and apixaban, though the data around that are not as obvious as those for warfarin or vitamin K antagonists.

We have the treatments there, but often you're asking what is the reason I need to treat this person? Is this person's portal vein thrombus causing ascites that is easily manageable with diuretics and they don't need to be treated? Or is this person's portal vein thrombus causing significant side effects, pain, discomfort that is better for this patient right now? So, I think having a patient-centered approach and shared decision-making around the risks benefits of treating the portal vein thrombus and as a hospitalist, my cop-out answer is always going to be "I'm going to discuss it with my hepatologist." I have the great privilege at working at, I guess, Kashlak Southeast hepatologists who see these patients long-term and can also help make that distinction of deciding if this person right now needs to be treated.

Monee: T hat's really good and piggybacking off the coagulopathy piece. I think this is on top of mind of a lot of hospitalists who are working with the subspecialist for procedures and things. Talk to us about the INR and FFP administration in patients that need these.

Suchita: [laughs] I believe in high-value care as most of us as hospitalists do. So, we don't want to do things excessively and have to ask ourselves what's the evidence here? So, INR is a number and that's it. It doesn't actually reflect true clotting function. In order to do that, we have to check a ROTEM or rotational thromboelastography to really measure how that clot is forming. Then INR is based on factors like what? 2, 5, 7, 9, 10, protein C, protein S, something about the clotting cascade I learned first year in med school and promptly forgot. But I think that the INR reflects liver synthesis dysfunction.

It can be a marker of a bleeding state, but it also doesn't capture the fact the person has a higher risk of clotting. So, treating just a number isn't helpful. So, their guidelines actually support no routine administration of FFP or platelets before a diagnostic paracentesis. Most of our patients who have a diagnostic paracentesis are going to have a small procedure, low bleeding risk, minimal fluid removed for diagnosis, and then the risk of procedure itself, especially when you use point-of-care ultrasound to localize is extremely low.

So, the Journal of Hospital Medicine says things we do for no reason of routine administration of blood products before a diagnostic paracentesis. The AASLD 2021 guidelines say don't routinely correct a perceived coagulopathy before a diagnostic paracentesis. I think a takeaway for us as hospitalist is that "The INR is just a number, treat the patient in front of you."

Monee: I love this permission structure.

Meredith: And I was going to say, you mentioned this during your talk, and that was actually mentioned in another talk I went today as well. So, it's definitely been a recurring theme. I think, going back to the SBP conversation and your need for a diagnostic para, you talked a few minutes ago about reason you're doing the diagnostic para solely for-- it's a cellular diagnosis, you can't make that diagnosis clinically. And I think during the talk too, you talked a little bit about the findings from your cell count and everything. I think it's always helpful to go through what those are, those findings that help guide your next decision-making. So, if you could do that for us, that'd be great.

Suchita: Yeah. So, for our patient, he came in with new-onset ascites. So, first step is we presume this is due to underlying liver disease. We have to confirm that. So routinely checking on the first time you're doing the evaluation, checking a serum ascites albumin gradient. So, what's the level of albumin in the serum? What's the level of albumin in the fluid that you're checking? So, a serum ascites albumin gradient greater than 1.1 reflects a transudate so that's often due to liver disease. And then the next decision point there is what's your fluid total protein? If a fluid total protein is greater than 2.5 that's highly suggestive it's due to cardiac etiologies and not liver etiologies.

So, first step is confirming that the fluid in the belly is actually due to a transudative process related to liver, so cirrhosis-related ascites because lots of other things can cause fluid in the belly. And then you have to think about what's my cell count culture, Gram stain, and does this person have spontaneous bacterial peritonitis. The key point here is that you don't have to have bacterascites or bacteria in your ascites that's cultured out in order to have SBP and treat for SBP.

If you think about it, you're culturing from-- someone's got seven liters of fluid in their belly, you're drawing off 50 cc of fluid, putting it into two 10 cc blood culture bottles, and sending it down to a lab. And the likelihood of your sampling error being there, you're probably not going to find bacteria if they're just swimming around in low numbers, but what you are going to find is a cellular response to it. So, a high cellularity of greater than 250 PMNs is a definition of SBP. And then you have to treat that, so empirically with third-generation cephalosporins, we generally use 1 g of ceftriaxone a day for five to seven days.

If a patient isn't getting better after about 48 hours, then thinking about resistant organisms and treating with pip/tazo or meropenem or another carbapenem and switching up the antibiotics, or repeating the diagnostic paracentesis, seeing if you can culture something out if the patient's clinically not improving.

Meredith: And are there any risk factors for someone to be more likely to have an MDRO? Like, I would think if they've had repeated taps or things like that, they might be at higher risk, but I don't know if that actually exists or I'm just making that up.

Suchita: I don't know if you're making it up because I actually don't know that answer. But I think that as we look at antibiotic resistance in general, it's a growing problem, which is why the

AASLD guidelines are more stringent around who needs prophylaxis for SBP. It's not any comers with ascites get prophylaxis with antibiotics against SBP. It's people who have illness, like significant illness, high Child-Pugh score, high total bili, high INR high creatinine. People who are more likely to get sick if they get SBP. They're the ones who need the prophylaxis against SBP. People who have already had it, have proven they can get it, and they should get prophylaxis. And so, we usually use ciprofloxacin 500 mg a day or trimethoprim and sulfa one double-strength tablet daily. Obviously modifying that based on age, creatinine, and other risk factors.

And choosing the risk-benefit for your patient if they are going to be at risk for an MDRO. If you're culturing something out that isn't sensitive to ciprofloxacin, probably don't pick that as your prophylactic drug. People have used metronidazole and other medications as well.

Monee: One of the things that I hadn't realized before is yes, like creatinine, Tbili. Actually, I don't think I'd realize that either, but also like the low protein ascites being one of the higher risk factors. I don't know if I saw a definition. Are you familiar with what the definition of low protein? I'm just curious.

Suchita: Yeah. A total protein of less than 1.5 in the fluid is considered low protein. So, low-fluid protein is, by AASLD guidelines, less than 1.5. And the reason that isn't one of the risk factors that predisposes somebody to SBP is you have low oncotic pressure. So, the translocation of bacteria is going to be more likely in that situation. So, that's your cut-off when you are checking your total fluid protein.

Monee: Okay. I think the guidelines also talk a lot about how they're just predisposed to more infections in general, which I found to be things that I should probably have recognized before. But that was nice to see in writing. So, we've done SBP, we're talking about portal vein thrombus and recentering with ascites, talk a little bit about diuretics and sort of like where to start, where to go, that kind of stuff.

Suchita: I love this topic because it's purely based on physiology. We talked about the peripheral vasodilation. We talked about the impaired renal blood flow. Because of that, you have the upregulation of the renin-angiotensin-aldosterone system and then increased plasma renin activity leading to salt and water retention. So, all that fun physiology is simply there to say that the target should be your RAAS system for diuretic management here in cirrhosis.

So, we have the upregulation of the renin-angiotensin-aldosterone system. So, the increased plasma renin activity leading to salt and water retention. So, the target here is the physiology. Spironolactone is the diuretic of choice in people with cirrhosis with ascites. And you start it at about 100 mg a day and the furosemide in a ratio of 40:100. So, 40 mg of furosemide with 100 spironolactone that's there for maintaining the potassium balance.

Spironolactone alone has been shown in studies to be effective in fluid management in people with cirrhosis. If you are picking one medication to start somebody on for cirrhosis with ascites, it should be spironolactone, which is counterintuitive to everything we hear about fluid management for other disease processes. But that's a fun of the physiology here in the liver, and then the potassium balance can be managed with the furosemide.

Meredith: We've talked a little bit about diuretic therapy. I know we use albumin in liver disease, but I always feel like albumin is sort of magic. Like, you're just, like, giving it and hoping for the best. But you talked a little bit about how there're indications and evidence that's driving when albumin is useful. So, especially for this patient with our ascites, if we could go through that a little bit?

Suchita: Yeah. I'd love to refer everyone to Suchita Sata et al. in Journal of Hospital Medicine Clinical Progress Note" Intravenous Human Albumin in Patients With Cirrhosis. I'm just joking. But, yes, you should go read that article. There are three evidence-based indications and guidelines supported indications for the administration of IV human albumin in people with cirrhosis. And when I say albumin, I mean 25% hyper-oncotic albumin, not the 5% version. This is the stuff that works.

Monee: Weak sauce.

Suchita: Yeah. If you're going to pay good money for this human albumin product, use the stuff that's going to actually make a difference from the oncotic pressure standpoint. So, there's three reasons. One is the prevention of paracentesis-induced circulatory dysfunction. And so, if you have somebody with ascites and you're doing large volume paracentesis, that's defined as greater than 5L, you need to replace some of that volume with albumin on the order of 6 to 8 g/L of ascites removed.

So, if you're taking out 5 L, if albumin is coming in a 25-g vial at your hospital like it is at mine, you're probably going to give them either 25 or 50. So, 6x5 is 30, you can err towards 25 or if you're doing 8 L, 8x5 is 40, you can probably err towards 50-g vial.

You don't want to waste albumin, it's expensive, has a short shelf life once it's hung for administration. So, the math here is 6 to 8 g/L of ascites removed. And of course, 5L is an absolutely arbitrary cut-off. Some people say 4L. The key here is who is at risk for paracentesis-induced circulatory dysfunction. Those are people who already have low blood pressure, that's people who already have impaired kidney function. And the reason we give albumin is to bring more blood flow to the kidneys, those selfish, selfish organs.

It's about the RAAS system and having the kidneys not perceive a prerenal state. So, they have to get more fluid brought to them in the form of us giving them albumin to support their circulatory system. So, that's the number one reason to give albumin. Number two reason is during the treatment of spontaneous bacterial peritonitis, you want to prevent the circulatory dysfunction there. So, someone who has SBP, standard of care to do 1.5 g/kg on day one and then 1 g/kg on day three. And that's for someone who has paracentesis-proven SBP. It helps reduce the risk of hepatorenal syndrome with acute kidney injury.

Yet another reason why it's so important to do that diagnostic paracentesis upfront. And then the number three guideline-supported reason for albumin is for hepatorenal syndrome, diagnosis, and treatment. So, you give a dose of 1 g/kg for a couple of days, see if you have an improvement with that volume expansion, and then you can continue it with 25 to 50 g daily. There is no definite endpoint. The answer is when it gets better, when the kidney function gets

better, which may or may not happen with or without a transplant. So, hepatorenal syndrome gets more blood flow to the kidneys in the form of support through albumin.

Monee: Yeah, so hepatorenal syndrome is actually a good segue into one of our next cases. So, Ms. Jackson, she's 51, she's got cirrhosis, ascites and she came in with some dizziness and fatigue. She's on a diuretic Ancipro. She's hemodynamically stable, but we find that her creatinine has bumped from her baseline from 1 to 2.5. And her sodium, which is normally in the low 130s is down to 126. So, obviously, when someone with cirrhosis comes in with AKI, I'm already thinking about hepatorenal syndrome. But what's my first thing that I need to do?

Suchita: I would love to do all these things parallel, but you would stop the diuretics, hold those diuretics on admission because again, it's all about supporting the blood flow to the kidneys. So, we hold the diuretics, to prevent worsening of the volume status. And then of course, you've already done, in this case, the right upper quadrant ultrasound with dopplers, you've done your diagnostic paracentesis, you've thought about the reasons this person has an acute kidney injury. And then you transition towards supporting the management of AKI. So, you stop diuretics and then you volume expand. So, we go back to the administration of albumin for hepatorenal syndrome with acute kidney injury.

And then often what's happening is these people have low blood pressure systemically, and that is also driven by portal hypertension. So, octreotide is a somatostatin analog that will help shunt blood back into circulation towards the kidneys out of the portal system. So, you can give octreotide a 50-mcg bolus, a 50 mcg/hr infusion. Octreotide, which is a somatostatin analog you can give to help shunt blood back into the system, and then midodrine to support the peripheral blood pressure, so essentially an oral pressor.

So, my mnemonic is MAO, midodrine, albumin, octreotide, that's how you volume expand and stopping diuretics to help support blood flow to the kidneys or hepatorenal syndrome. We don't have terlipressin mostly in the United States. It was approved by the FDA in September of 2022. I don't even know if my hospital has it yet. But that is a medication that is essentially a vasoconstrictor to help support blood flow to the kidneys. And the other option is norepinephrine as an adjunct if MAO isn't working well enough.

Meredith: And do you have to albumin challenge them first or can you do midodrine, albumin, and octreotide all together?

Monee: Because I feel like that's what I have done in practice, but I don't know what's the evidence for that or not.

Suchita: So you have to ask, are you treating hepatorenal syndrome with acute kidney injury or are you treating acute kidney injury by itself? So, it's hard to tease that out in practice because someone on diuretics can become volume depleted alone without the neurohormonal changes that are associated with hepatorenal syndrome. So just volume expansion with albumin or that albumin challenge upfront on day one is sometimes helpful in reversing the AKI along with holding their diuretics. That's the 1 g/kg dosing for the first two days.

Obviously, if they're not getting better or if they're getting worse fast or if they have a significant AKI that you're very concerned about with low urine sodium, so you already have concerns about excessive sodium retention, then you think about upfront administration of midodrine and octreotide. I think it's a case-by-case discussion and often we're consulting nephrology in addition to your hepatology colleagues, because if this doesn't get better, they may need to progress towards transplantation, which is one of the only cures for HRS-AKI and that might be both liver and kidney transplant.

Monee: One of the things that I found to be, I don't know if confusing is the right word, but in reading the guidelines, especially going to the European guidelines, they very explicitly, if I remember correctly and I could be wrong, talk about how midodrine and octreotide are not as effective as, like say, a norepi or terlipressin. So why do we use it so much? One, did I get that right? And two, why do we use it so much?

Suchita: Absolutely. So, the studies are best in terlipressin, the actual outcomes both in morbidity and mortality and the actual kidney function. We haven't had terlipressin here in the United States. So that's a short answer of why we haven't used that. I'm a hospitalist. I don't practice in the ICU. It's really hard to get somebody into the ICU just for numbers of creatinine. So, the version is an oral pressor of midodrine. What can you get away with on the floor?

Often what will happen is the midodrine itself with the octreotide isn't causing enough improvement. Then they will progress to be moved to the intensive care unit for the norepinephrine infusion. So, I think it's more just a logistics thing of practicing the evidence-based medicine we can in the place that we can, the best that we can while thinking about being stewards of overall healthcare resources as well.

Monee: Yeah, I feel like I've been reading about terlipressin for so long. So, when you mentioned in your talk it was approved, I, like, did a little happy dance, it's pretty exciting.

Suchita: Yeah, it's approved. Is it available, affordable, and accessible is the question. It's on the horizon.

Meredith: So, coming back in for Ms. Jackson, let's say she's on hospital day two and the nurse is calling you saying she had some hematemesis. And now we're going into the spectrum of GI bleed.

Suchita: I think that in general, we do a fair number of just early management of GI bleed. But in patients with cirrhosis, I think that there's just a lot more things you have to think about because it won't just be a peptic ulcer.

Meredith: And it could be a peptic ulcer.

Suchita: It could be. Patients with cirrhosis are allowed to bleed from wherever they want to bleed from. The one that we're most concerned about though, of course, is esophageal varices. Because those are the scary, fast, brisk bleeds that cause life-threatening hemorrhage with potential risk for AKI and all the other negative complications. So, you're calling your GI colleagues for the procedure and the procedures they'll offer of course include banding or

injecting glue and dealing with the varices and fixing it. But what can we do while awaiting for our GI colleagues to come in and work their magic? Supporting the blood pressure? So, if they're on things like diuretics or beta blockers to hold them in that moment, patients with cirrhosis or varices are often on a nonselective beta-blocker to prophylax against the bleeding.

We want to pause it in that acute setting. You want to resuscitate, but not too much. So, the perfect goldilocks amount to hemoglobin target of between 7 and 9. You want to give them enough blood but not too much to make those varices too juicy to bleed and all the negative side effects of excessive blood transfusion. And then you want to think about what is happening now with all this blood rushing through the GI system, all that bacteria that's coming with it. Are we going to be at risk for SBP? So, we actually empirically treat patients for SBP with a gram of ceftriaxone for five days when they have a GI bleed with ascites. So, the big key points here are what do you think is bleeding? Let's go visualize that, let's deal with that with our GI colleagues, but in the meantime supporting them with the prophylactic antibiotics and the blood pressure support.

Meredith: And when do you start considering like, beta blocker?

Suchita: Once a patient has had a bleed and they've had their EGD and they have varices shown on there and they're now hemodynamically stable, their blood pressure is beautiful again, you've saved their life, congratulations. You're thinking about how I prevent this from happening again. So, nonselective beta-blockers are indicated for prevention of recurrent variceal bleeding, but they have to have the blood pressure room for it. And I say nonselective beta blockers, but I'll lump in with propranolol and nadolol. I'll lump carvedilol into that category, which is technically not one of those, but it has additional benefits and has been studied in some trials to actually be one of the best. But it has such a big blood pressure effect, patients can't tolerate it as often.

Monee: Got it. Okay, so we had the GI bleed, we did all the stuff that we need to do, work up and stuff and Ms. Jackson is just having a really rough go of it. And day four she's like recovered from her bleed, everything's stabilized, but now she's like super confused, very confused. So, obviously we worry about hepatic encephalopathy, so how do we deal with that? And how many times am I going to check the ammonia level.

Suchita: The answer is never check ammonia in someone with chronic liver disease, that is a thing we do for no reason. The reason being that hepatic encephalopathy or portosystemic encephalopathy is a clinical diagnosis. Ms. Jackson is confused. Is it confusion because of her liver? Most likely in someone who's ill with decompensated cirrhosis, if they have asterixis on exam and have some day-night reversal or increased somnolence, it's pretty much hepatic encephalopathy and you treat it. If her ammonia level came back as stone cold normal and she still had asterixis is on exam, you would probably still treat with lactulose.

So, the treatment for hepatic encephalopathy is a non-absorbable disaccharide. We use lactulose because it's just available and I like to frame this as thinking about it. If you have someone come in with heart failure that's decompensated, you don't use their home dose diuretic. That is one of the biggest pitfalls I see is that we put them on lactulose and say to the nurse, okay, titrate to three bowel movements a day, here's your BID lactulose. And then four days later, they're still encephalopathic it's because we haven't done enough upfront.

So, if someone comes in with volume overload from heart failure and you give them IV diuresis and you ramp up their dose and you treat aggressively, same philosophy applies to hepatic encephalopathy. Titrate the lactulose to effect, make them poop, poop till they're clear, and the lactulose frequency, obviously, you can't really do more than, like, q2 hours, and that's hardly kind to the patient, your nurse, and everybody else who is downwind of that room. But treat the symptoms and treat aggressively upfront. That way you don't have to be as aggressive down the road.

There are other therapies that have been examined. Rifaximin, of course, is a medication we use for recurrent hepatic encephalopathy. Make sure your patient can afford it and access it. And it often requires prior authorization because it is brand name only. Zinc is a cofactor in ammonia metabolism and so that can be an adjunct. Polyethylene glycol, 4L of a colonoscopy prep has been studied in one small trial to be as effective, if not more effective than lactulose. But that's a lot of fluid for someone to drink if they are confused and at risk for aspiration and they don't have oral access with an NG tube. And then there are other things like LOLA coming out down the pipeline, which is L-Ornithine L-Aspartate that physiologically makes sense from the hepatic encephalopathy standpoint, but my go to is lactulose and making them poop.

Meredith: I feel like Ms. Jackson's had a bit of a run of it in the hospital. And I always struggle with goals of care discussions in end-stage liver or patients with cirrhosis in general because it's such a process that they're going through and you're still delivering treatment along the way. And so, I was hoping you could teach us a little bit about how you frame that conversation with your patients to introduce goals of care conversations with them?

Suchita: Yeah, cirrhosis is associated with really negative health-related quality of life metrics. It is a chronic disease that people have to live with and all the things we talked about therapies, diuretics, you have to make them pee. lactulose, you have to make them poop. This is not a comfortable illness to live with and the treatments are intense. We can modify a lot and we can help prolong life. And many patients do have cured disease through transplantation and that's if they are candidates for transplant. So, my first approach is an early referral to hepatology so they can be considered for transplantation upfront.

And that is so key to making sure they get all the guideline-directed therapies to prevent progression. We've talked about a bunch of them today, but I think the hepatologist can also think about liver transplantation. But then in addition to thinking about transplantation, one is your patient knowing that they are ill? Have we shared that information with them? We talk about MELD scores and risks and mortality all the time amongst ourselves. But does a patient know, even though they feel fine from their chronic liver disease, that they have a high 90-day mortality with their high MELD score?

So, using that information, sharing it, and having that shared decision-making or at least conversation with your patient and symptom management, make them more comfortable as they're dealing with this awful chronic disease. And then thinking about a discussion of advanced care planning earlier. Because not only is not everyone a transplant candidate that might not be the right choice for people even if they are. Chronic liver disease is a fourth leading cause of death in the United States as of a few years ago and it is becoming more and more

common, especially with the uptick in nonalcoholic fatty liver disease-related chronic liver disease.

We're doing great with curing hepatitis C. We still have plenty of room to go. But NASH is becoming more and more frequent. So, I think having that conversation about symptoms, priorities, and acknowledging that this is a severe end-stage disease that isn't as obvious as something like end-stage heart failure but is as significant of a trigger point for discussion of goals of care.

Meredith: And I think you talked making sure the patients a little bit more comfortable while they go through a pretty difficult process. What are some of the medications you go to for symptom management?

Suchita: You can still use acetaminophen up to 2 g a day total. Do not use NSAIDs if you can avoid them because of the RAAS activation and the salt and water retention. Same reason we don't like to use NSAIDs in people with heart failure. So, acetaminophen is a reasonable first step for pain management. Opioids are not contraindicated. We like to be thoughtful around opioid use for everybody and some of synthetic opioids are better tolerated than things like morphine.

The other symptoms include muscle cramping from diuretics. So, in addition to making sure the magnesium and potassium levels are replete, we have to think about things like baclofen, methocarbamol, quinidine have all been suggested, but baclofen might be the first go to for muscle cramping and for pruritus or the itchiness that comes with hyperbilirubinemia using emollients, topicals, there have been plenty of other medications suggested, I think. I'm not a specialist in symptom management, but being thoughtful about what the symptoms are and asking about them and asking your patients if that is something they want another medication for or if they can tolerate it because a medication and pill burden is pretty high. If you think about diuretics, lactulose, rifaximin, a nonselective beta blocker, all of the other things that need to be present for evidence-based therapy.

Meredith: And do you worry at all on the baclofen or in your practice, have you seen that cause any confusion or altered mental status that then drives you down this, like, encephalopathy pathway, and then you're like, what did I do?

Suchita: [crosstalk] -Iatrogenesis, no baclofen in CKD? I think Dr. Matthew Sparks, who was on a bunch of Curbsiders episodes, would be thrilled with me saying that. So, no baclofen in CKD. It's renally excreted. The caution is less obvious for someone with liver disease alone, but being aware of what your renal function is very important.

Meredith: Wonderful. I think we've hit, like, a lot of good highlights tonight. And Suchita has to go see her lovely child. So, do you want to let us know some take-home points you want to make sure the audience got from all of this?

Suchita: Thanks. I would love to leave everybody with the key exhortation that, one, we need to approach decompensated cirrhosis in the hospital in a systematic way. There are guidelines that drive medical therapy just like we do for heart failure. We have to be systematic and think about

all the reasons someone has decompensation. So, be systematic about getting right upper quadrant ultrasound, being systematic about doing the diagnostic paracentesis, thinking about all the etiologies that trigger and all the signs and symptoms of decompensation, because that leads to all the guidelines we have to meet to provide evidence-based, high-value care for our patients.

My second takeaway will be albumin has a great wealth of evidence for three indications of prevention of paracentesis-induced circulatory dysfunction, treatment of spontaneous bacterial peritonitis, and then diagnosis and evaluation of hepatorenal syndrome. So, use the guidelines. Don't excessively waste albumin because there are significant harms associated with it for your patients in addition to financial toxicity.

And then three, think about the next step in planning for your patient with cirrhosis. Just because you stabilize them during this hospitalization, you have to ask yourself, what are we doing next for this person? So, early referral to transplant centers and hepatologists as well as early discussions around palliation and goals of care, which is not necessarily divergent things. Palliation is a process and can be done at all stage of the illness even if somebody is being considered for transplantation.

Monee: Fantastic. Thank you so much for taking the time to talk with us right after you gave your talk, frankly. We really appreciate your time and anything you want to plug other than your awesome article in JHM about albumin.

Suchita: I love the opportunity to meet you guys. And Society of Hospital Medicine has been a great place for my own growth professionally and personally. And so, I'm going to plug coming to these conferences, joining SHM, making it a professional home, and it's just been an absolute joy to reconnect with friends all across the country here at this conference.

[music]

Meredith: This has been another episode of The Curbsiders bringing you a little knowledge food for your brain hole.

Monee: Yummy.

Meredith: Still hungry for more?

Monee: Yep.

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available for CME Credit for all healthcare professionals through VCU Health at *curbsiders.vcuhealth.org*. A special thanks to ourselves for writing and producing this episode as well as the whole team with Curbsiders. Our technical production is done by the team at Pod Paste, Elizabeth Proto runs our social media, and Stuart Brigham composed our theme music. Until next time, I've been Monee Amin.

Meredith: And I'm still Meredith Trubitt. Thank you and goodnight.

[Transcript provided by SpeechDocs Podcast Transcription]