Jessica P.E. Davis
January 2023

Handy Numbers for DC VA Hepatology Services

Transplant Coordinator on Call: 202-213-3562

Liver fellow on call:

7:00-17:00: 202-359-3307

17:00-7:00: see GI call schedule on VA homepage

Hepatology attendings:

Jessica Davis, jessica.davis2@va.gov, personal cell 850-544-5249

Atoosa Rabiee, Atoosa.rabiee@va.gov, personal cell 443-468-5228

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Post-liver Transplant Elevated Liver Enzymes

Common Etiologies

- Biliary Stricture
- Hepatic artery thrombosis/stricture
- Rejection (sometimes due to medication nonadherence)
- Infectious – CMV, EBV, VZV, HSV, HCV, HBV, HAV
- DILI – new antibiotic, acetaminophen

Evaluation

- History: immunosuppression compliance, new medications, prior rejection
- Imaging: RUQ US WITH hepatic artery doppler**essential to r/o HAT
- Labs: LFTs, immunosuppression troughs, HAV IgM, HBsAg, CMV PCR, EBV IgM, HSV IgM, VZV PCR/IgM, HCV VL
- MRCP if cholestatic pattern of LFT abnormalities
- Consult Hepatology

Management Pearls

- Check daily LFTs and relevant immunosuppression troughs
- Involve transplant team
- If work-up unrevealing may need early liver biopsy
- If concern for biliary stricture may require ERCP even w/normal MRCP as MRCP are less sensitive post-transplant
- If concern for hepatic artery thrombosis (HAT) need to involve surgeons/IR asap
- If biopsy consistent with rejection, treatment will be increased immunosuppression. The degree of additional IS needed will be proportional to severity of rejection. Consider restarting infectious prophylaxis for PJP and/or CMV if patient to be on prolonged corticosteroids or receive other highly immunosuppressive treatments (e.g. ATG).

References

Toniutto P, et. al. An Essential Guide for Managing Post-Liver Transplant Patients: What Primary Care Physicians Should Know. Am J Med. 2022 Feb;135(2):157-166.

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Post-liver Transplant with Hyperkalemia

Pathogenesis

- Worsening kidney function post-transplant
- Medication side effects – common actors are Calcineurin inhibitors (CNI), Bactrim

Evaluation

- Medication and diet history – any new meds, any high potassium foods?
- EKG

Management Pearls

- Urgency of therapy:
    - K+6.5 or greater in any patient needs rapid lowering
    - K+ with clinical signs (EKG changes, muscle weakness/paralysis) needs rapid lowering
    - K+ 6 or greater in setting of oliguria/HD needs rapid lowering particularly if ongoing tissue breakdown/potassium absorption
- Monitor patients with continuous tele + serial EKG
- Initial urgent treatment with Ca++, insulin, and glucose +/- furosemide and albuterol
- Longer term therapy:
    - Advise low potassium diet
    - Reduce doses of CNI if possible
    - Sodium zirconium cyclosilicate (SZC/"Lokelma") is preferred cation exchanger for long-term therapy, can start at 10 mg TID x 48 hours then 10 mg daily

References

Packham DK, et. al. Sodium zirconium cyclosilicate in hyperkalemia. N Engl J Med. 2015 Jan 15;372(3):222-31.

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Post-liver transplant Common Medication Side Effects

Side Effect	Culprit Agents	Approach
Bone Marrow Suppression Pancytopenia, leukopenia, neutropenia, anemia, thrombocytopenia	Antiproliferative agents (MMF, AZA, MTOR)	• Switch to different agent/dose reduce • G-CSF/GM-CSF to treat severe neutropenia • Transfuse for goal hgb of 7, evaluate iron stores and assess need for IV iron/epoetin infusions
Gastrointestinal symptoms Nausea, vomiting, diarrhea	Antiproliferative agents (MMF, AZA)	• Rule out other causes (c diff, CMV) • Consider switching to Myfortic (enteric-coated)
Neurotoxicity Tremors, HA, seizures, delirium, PRES	CNI	• Trial magnesium supplementation • Switch to Envarsus* for tremors (peak-related) • Consider switch to cyclosporine from tacrolimus for PRES
Nephrotoxicity AKI, CKD	CNI	• Use renal-sparing regimens at time of transplant • Combination therapy with antimetabolite to allow lower CNI target trough
Increased Infections Viral and bacterial	All IS Agents	• For severe infections may hold antimetabolic/reduce IS WITH involvement of transplant team

Abbreviations: AKI (acute kidney injury), AZA (azathioprine), CKD (chronic kidney disease), CMV (cytomegalovirus), CNI (calcineurin inhibitors), CSA (cyclosporine), HA (headache) IS (immunosuppression), MMF (mycophenolate), PRES (posterior reversible encephalopathy syndrome)

References

Rabiee A, and Davis J. “Brief overview of immunosuppression and their side effects after liver transplantation.” *Chronic Liver Disease*. 2023. In press.

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Post-liver transplant Common Medication Interactions

	Increase levels of IS					Decrease levels of IS		
	Azoles	Calcium channel blockers	Macrolide antibiotics	Protease inhibitors	*Allopurinol (AZA only)*	St. John's Wort	Antiseizure medications	Cholestyramine iron prep
	Fluconazole Voriconazole	*Diltiazem verapamil*	*Clarithromycin Erythromycin*	*Paxlovid, ritonavir*			*Phenobarbital Phenytoin*	
CNI	TAC ↑ CSA ↑	TAC ↑ CSA ↑	TAC ↑ CSA ↑	TAC ↑ CSA ↑		TAC ↓ CSA ↓	TAC ↓ CSA ↓	
mTORi	SRL ↑	SRL ↑	SRL ↑	SRL ↑		SRL ↓	SRL ↓	
AZA, MMF					AZA ↑			AZA ↓ MMF ↓

- IS: Immunosuppression; CNI: Calcineurin Inhibitor; TAC: Tacrolimus; CSA: Cyclosporine; MMF: mycophenolate; AZA Azathioprine

- Calcineurin inhibitor levels are increased by cytochrome P450 inhibitors and decreased by cytochrome P450 inducers.
- NB: this list is not comprehensive and all drugs should be reviewed for interactions prior to prescribing.

References

Adapted from Rabiee A, and Davis J. "Brief overview of immunosuppression and their side effects after liver transplantation." *Chronic Liver Disease*. 2023. In press.