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Managing TB and HCV in DCLD (CTP B): A Balancing Act Between ATT and DAA

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CASE VIGNETTE

A 51-year-old woman with type 2 diabetes and chronic HCV infection presented with a 3-month history of productive cough, fever, abdominal distension, and dyspnea. Evaluation revealed **decompensated chronic liver disease (DCLD), Child-Pugh B (score 9)** with high HCV viral load (7,12,000 IU/mL). Imaging showed bilateral pleural effusion and ascites, and sputum CBNAAT confirmed **rifampicin-sensitive pulmonary tuberculosis**.

Given her advanced liver dysfunction, initiating both **anti-tubercular therapy (ATT)** and **direct-acting antivirals (DAA)** posed a significant challenge. ATT (especially isoniazid and rifampicin) carries a high hepatotoxic risk, and the use of DAAs in decompensated cirrhosis also requires caution. Following stewardship principles, the team opted to **initiate ATT first**, with close monitoring of liver function, and **defer DAA therapy** until completion of the intensive TB phase or stabilization of hepatic parameters.

Ques. In a patient with decompensated chronic liver disease (Child-Pugh B) who has active TB and HCV co-infection, which of the following best describes the recommended approach to initiating therapy?

A. Start ATT and DAA concurrently regardless of liver function.

B. Initiate ATT first and delay DAA until liver function stabilizes (usually after the intensive phase of TB treatment).

C. Begin DAA first to improve liver function before starting ATT.

D. Defer both therapies until liver enzymes normalize completely.

ANSWER: B. Initiate ATT first and delay DAA until liver function stabilizes (usually after the intensive phase of TB treatment)

COMMENTS

In patients with DCLD (CTP B), the risk of drug-induced liver injury is high. As a stewardship principle, it is generally recommended to **prioritize anti-tubercular therapy**—given the urgency of treating active TB—and delay DAA initiation until liver function stabilizes. Concurrent initiation of ATT and DAA is generally not advisable in this setting due to:

- **Increased Hepatotoxicity:** The combined hepatotoxic effects of ATT (particularly isoniazid) and DAA may exacerbate liver injury.
- **Drug-Drug Interactions:** Rifampicin, a cornerstone of ATT, is a potent enzyme inducer and can reduce the efficacy of DAAs.
- **Clinical Stability:** Patients with CTP B have limited hepatic reserve, making them more vulnerable to additional insults.
- However, in rare scenarios where TB is less severe or liver function remains relatively stable despite DCLD, and where rapid HCV clearance is critical (for example, to qualify for liver transplant), concurrent initiation may be considered under close monitoring and in a multidisciplinary setting. Such decisions must be individualized, with rigorous surveillance of liver enzymes and clinical status.
- Factors Influencing Treatment Prioritization in HCV–TB Co-infection

Start ATT First	Start DAA First	Start Both Together
- **Active TB with significant symptoms** or radiological evidence of progression	- **Compensated or early DCLD** with high HCV viral load and relatively **mild TB**	- **Stable Child-Pugh B** patient with **mild TB and HCV**, needing rapid viral suppression (e.g., transplant listing)
- Child-Pugh B/C with **limited hepatic reserve**	- HCV-induced hepatic decompensation where **TB is latent** or indolent	- When both infections are active but **drug interactions can be managed** and patient is under **close monitoring**
- ATT is **life-saving** and delays increase mortality risk	- DAA can potentially **improve liver function** and **enable safer ATT** later	- Managed in **high-resource settings** with access to therapeutic drug monitoring (TDM) and expert hepatology input
- High risk of hepatotoxicity from isoniazid/rifampicin **requires deferral of DAAs**	- When rifampicin **not immediately needed** or replaced with a DAA-compatible ATT regimen	- **Multidisciplinary care** available and regular LFT surveillance possible

Stewardship Interventions:

- **Sequence Therapy Based on Urgency and Tolerance:**Prioritize the initiation of **ATT** to control the active TB infection, as delayed treatment can be life-threatening. DAA therapy should be **deferred until hepatic function stabilizes**, typically after the intensive phase of TB therapy (first 2 months), or once liver enzymes normalize.
- **Multidisciplinary Coordination:**Collaborate with hepatologists, infectious disease specialists, and the antimicrobial stewardship team to ensure therapeutic decisions are individualized and evidence-based.

- **Rigorous Monitoring:**Implement close and frequent **liver function monitoring** during ATT. This helps detect early signs of hepatotoxicity and guides the safe introduction of DAAs at an appropriate time.

- **Tailored Treatment in Special Scenarios:**In selected cases—such as those being evaluated for **liver transplantation**, or where TB is clinically less severe—**simultaneous initiation of ATT and DAA** may be considered. This must occur under **strict monitoring**, with clear clinical justification and consensus among specialists.

REFERENCE

1. Lomtadze N, Kupreishvili L, Salakaia A, Vashakidze S, Sharvadze L, Kempker RR, Magee MJ, del Rio C, Blumberg HM. Hepatitis C virus co-infection increases the risk of anti-tuberculosis drug-induced hepatotoxicity among patients with pulmonary tuberculosis. PloS one. 2013 Dec 19;8(12):e83892.
2. Kim WS, Lee SS, Lee CM, Kim HJ, Ha CY, Kim HJ, Kim TH, Jung WT, Lee OJ, Hong JW, You HS. Hepatitis C and not Hepatitis B virus is a risk factor for anti-tuberculosis drug induced liver injury. BMC infectious diseases. 2016 Dec;16:1-7.
3. Ashkin A, Alexis A, Ninneman M, Rafael Calpena Rico, Ashkin D, Peloquin CA. Concomitant Treatment of Tuberculosis and Hepatitis C Virus in Coinfected Patients Using Serum Drug Concentration Monitoring. Open Forum Infectious Diseases [Internet]. 2023 May 4;10(6).
4. World. WHO announces forthcoming updates on co-administration of treatment for drug-resistant tuberculosis and hepatitis C [Internet]. Who.int. World Health Organization: WHO; 2024