31st Annual Scientific Meeting of Indian National Association for Study of the Liver (INASL 2023)

LTx FOR ACUTE-ON-CHRONIC LIVER FAILURE: DON'T RUSH IT!

Dr Dharmesh Kapoor, Hyderabad

Acute-on-chronic liver failure (ACLF) is a dynamic syndrome associated with very high short-term mortality. Until 2013, there was no evidence-based definition of ACLF. However, a definition was later proposed based on the results of a large prospective observational European study, called "European Association for the Study of the Liver (EASL)–Chronic Liver Failure (CLIF) Consortium Acute-on-Chronic Liver Failure in Cirrhosis (CANONIC)" study.

The CANONIC study also found that: Identifiable precipitating events (e.g., bacterial infection, active alcoholism) are found in only 50% of cases of ACLF. Precipitating events may be initiators of ACLF but do not drive the outcome. ACLF is associated with systemic inflammation even in patients who do not have identifiable precipitating events.

When it comes to the treatment of ACLF stage 2-3, liver transplantation (LTx) has been shown to improve the survival of patients. It has been recommended that patients who recover from ACLF should also be listed for LTx, as the rate of mortality at 6 months is 40% to 50%. However, some of the factors can lead to escalation of care or futility of care after LTx, such as:

- Standard ICU consideration: Age, comorbidities, functional/nutritional status, severity of acute illness
- Liver-specific considerations: Severity of disease, indication of admission.

REDUCING DEATHS FROM ACLF IS A REALISTIC GOAL

Dr Rajiv Jalan, UK

- Patients with acute decompensated cirrhosis have high morbidity/mortality.
- Liver transplantation can save the lives of patients with ACLF.
- New therapies are under development for managing ACLF, like CARBALIVE, PRECIOSA, TLR4 antagonist, G-TAK, DIALIVE APACHE.
- Cirrhocare is a decompensated cirrhosis management in the community that provides early diagnosis, allows rapid intervention and reduces hospitalization; thus improving the quality of life.
- CARBALIVE are adsorbent beads whose unique physical structure gives functionality to remove macromolecules such as endotoxins which reduce inflammation and improves gut health.
- DIALIVE modifies the pathophysiological process involved in the pathogenesis of ACLF.

MANAGEMENT OF PATIENTS WITH HEPATIC ENCEPHALOPATHY

Dr Sunil Taneja, Chandigarh

- For the management of recurrent or persistent hepatic encephalopathy (HE), use a medical treatment like nonabsorbable disaccharides + rifaximin and avoid precipitating factors.
- In patients refractory to treatment, consider spontaneous portosystemic shunts (SPSS) (abdominal CT/MRI).
- In the presence of SPSS and model for end-stage liver disease (MELD) score ≤11, no significant PH-related complications and technical feasibility of embolization = consider embolization.
- In the presence of SPSS and MELD scores 12-14, consider each case individually. In the presence of SPSS and MELD score ≥15, significant PH-related complications, and technical difficulties for embolization = consider liver transplant.

NEWER THERAPIES IN HBV

Dr Anil Arora, New Delhi

- Complex hepatitis B virus (HBV) life cycle and current treatment are dependent on nucleos(t)ide analogues (NAs).
- A partial or functional cure is not enough, hence is crucial to target covalently closed circular DNA (cccDNA) for a complete cure.
- Entry inhibitors are approved for chronic hepatitis D virus (HDV), however, they do not address cccDNA.

- Attractive options for targeting cccDNA are – Inhibition of mini chromosomes and silencing transcription. Concerns over genomic stability are still hindrances.
- Post-transcriptional control – Antisense oligonucleotides (ASOs) and small interfering RNAs (siRNAs). Do not eliminate cccDNA, rebound post-treatment.
- Capsid assembly modulators (CAMs) are the best among the present novel therapies. They cause long-term suppression of HBV DNA and RNA.
- S-antigen transport-inhibiting oligonucleotide polymers (STOPS) and nucleic acid polymers (NAPs) have given promising results, however, need further studies.
- Good results have been obtained for TLR7, the combination of RIG with IFN, and promising results of vaccination in the phase III trial.
- Multiple combination strategies under investigation need larger and longer trials.

HBV RNA AND HBcrAg: BIOMARKERS OF DISEASE ACTIVITY IN CHB

Dr Norah Terrault, South California

HBV RNA and HBcrAg (Hepatitis B core-related antigen) are both biomarkers that are used to assess disease activity in chronic hepatitis B (CHB) infection. These biomarkers can help in determining the criteria to cess NA therapy. According to the Japanese HBV guidance, the criteria to cess NA therapy are: At least 2 years of administration of NAs. Undetectable serum HBV DNA level. Negative serum hepatitis B e-antigen (HBeAg) at the time of treatment cessation.

However, in case, when these criteria are met, hepatitis B surface antigen (HBsAg) and HBcrAg levels can be used to estimate the risk of relapse at the time of cessation. Some of the additional points to note about HBcrAg in CHB management are:

- HBcrAg and HBV RNA offer measures of cccDNA transcriptional activity, but not the amount of cccDNA.
- Limited diagnostic application – HBcrAg is strongly influenced by HBeAg status and the presence of PC/core mutations.
- Potential prognostic applications – Prediction of hepatocellular carcinoma risk in Indian patients and after HBsAg seroclearance; prediction of HBsAg loss in a subset of patients.
- Shedding new light on HBsAg seroclearance and liver-related risk that may occur after HBsAg loss. Most likely concept that will be useful in predicting outcomes after NA withdrawal. However, the only limitations are: Need to standardization, improve dynamic range and increase access/ease of use.

REFRACTORY ASCITES – NEWER CONCEPTS IN THE MANAGEMENT

Dr Rakhi Maiwall, New Delhi

Refractory ascites is a challenging condition where the accumulation of fluid in the abdominal cavity (ascites) does not respond to standard medical therapies. It is often associated with advanced liver cirrhosis and is a significant complication that can lead to poor quality of life and increased mortality.

Over the years, several newer concepts in the management of refractory ascites have been explored to improve patient outcomes. Transjugular intrahepatic portosystemic shunt (TIPS) prevents further decompensation and improves survival in patients with cirrhosis and portal hypertension. But some of the challenges associated with this method are: Patient selection; timing; risk of liver failure and HE; post-TIPS cardiac decompensation.

Another new concept is the alfapump system for patients with refractory ascites when TIPS is not feasible. This device is also used for patients with previously failed TIPS, portal thrombosis and associated cardiac dysfunction. This battery-operated device is subcutaneously implanted in the peritoneal cavity and drains ascitic fluid from the peritoneal cavity and into the urinary bladder. However, it has several limitations, such as cost, availability and risk of infection.

A liver transplant is the first treatment of choice for refractory ascites. Some of the other points that should be considered for managing refractory ascites are:

- Patients with low MELD scores should be considered.
- Patients with spontaneous bacterial peritonitis or hepatorenal syndrome should be prioritized.
- All other measures should be considered as bridge to transplant in the presence of refractory ascites.
- Simultaneous liver-kidney transplant for patients with concomitant chronic kidney disease stage 3b.
- Lastly, remember, other than these interventions, nutritional, frailty and palliation form an integral part of refractory ascites management.