Clinical Practice Guideline on the Management of Hepatic Encephalopathy (2022)

About the Guideline

- The guideline was developed by a panel commissioned by the European Association for the Study of the Liver and consisted of 36 reviewers including 24 hepatologists/gastroenterologists/ internists, five nurses, two methodologists, one neurologist, one neurophysiologist, one neuropsychologist, one neuroradiologist, one neuroscientist and one patient with a background in psychology interested in hepatic encephalopathy (HE).
- The guideline includes the definition, diagnosis, differential diagnosis and selected treatment options of HE. However, the pathophysiology of HE is not included.

Key Clinical Considerations

Become familiar with the recommendations and best-practice statements provided in this guideline, especially if you work in an acute care setting.

Classification Criteria

- HE should be classified as type A with acute liver failure, type B with portosystemic shunting, and type C with cirrhosis.
- Overt HE should be classified as recurrent if a patient experiences 2 or more episodes within a 6-month period, and persistent if the patient doesn't return to baseline function between episodes.
- Diagnostic accuracy and treatment can be impacted by identified precipitants, severity of mental alterations, and presence of portosystemic shunts.
- HE grading using the West Haven criteria is recommended when temporal disorientation is present.
    - Patients with no or mild neuropsychiatric abnormalities should be tested for covert HE diagnosis using a therapeutic or neuropsychological/neurophysiological test.
    - The Glasgow coma scale should be added in patients meeting grades III-IV West Haven criteria.
- In accordance with international guidelines for delirium, the term "acute encephalopathy" rather than "brain failure" should be used. In patients with acute-on-chronic liver failure the terms acute encephalopathy and hepatic encephalopathy are not synonymous.
- Underlying liver disease as a cause of liver failure should not be considered when defining or classifying HE, since numerous other etiologies (i.e., alcohol, diabetes, age or metabolic dysfunction) can influence the risk of HE.

Diagnosis

- Differential diagnosis of concomitant or pre-existing disorders causing neuropsychiatric impairment should first be identified when HE is suspected so that treatment will be accurate with improved outcomes.
- In patients with delirium/encephalopathy and liver disease:
    - Plasma ammonia levels should be measured since a normal value brings the diagnosis of HE into question.

  - CT scan or MRI of the brain is appropriate if there are diagnostic doubts or non-response to treatment.
- Screening for covert HE using available tools and local norms, such as the bedside Animal Naming test, should be performed in patients with cirrhosis and no history of overt HE.

Treatment

- Non-absorbable disaccharides is the recommended treatment for covert HE.
- Albumin dialysis may be considered in patients with liver failure and covert HE.
- Control of underlying liver disease progression, such as in alcohol misuse, and management of non-HE decompensation is recommended in patients with HE.
- Identification and management of precipitating factors should be sought in patients with HE.
- Due to the unpredictable clinical course and risk of aspiration of patients with overt HE grades 3 and 4, treatment should occur in the ICU.
  - Although no single marker can identify patients who will benefit from ICU admission, HE grade and Glasgow scores along with clinical judgement should dictate ICU admission.
- Liver transplant and referral to a transplant center for evaluation should be considered for patients experiencing a first episode of overt HE or having recurrent or persistent HE.
- For patients experiencing a first episode of overt HE, lactulose is recommended as secondary prophylaxis.
  - Lactulose should be titrated to obtain 2-3 bowel movements per day.
- Rifaximin is recommended as an adjunct to lactulose if the patient experiences 1 or more additional episodes of overt HE within 6 months of the first episode.
- To prevent HE, patients presenting with gastrointestinal bleeding should have rapid removal of blood from the gastrointestinal tract.
  - This can be accomplished by naso-gastric tube administration of lactulose or mannitol, or lactulose enemas.
- Rifaximin is suggested for prophylaxis of HE prior to non-urgent transjugular intrahepatic portosystemic shunt (TIPS) placement in patients with cirrhosis and previous episodes of overt HE.
  - Further study is needed for the use of non-absorbable disaccharides as a stand-alone treatment or as combination treatment.
- Discontinuation of anti-HE therapy should be based on the individual patient's response, improvement of liver function and nutritional status, and in whom precipitant factors have been controlled.
- Routine zinc supplementation is not recommended due to the conflicting evidence of zinc supplementation in HE patients.
- Vitamin/micronutrient deficiencies, whether demonstrated or suspected, should be treated in patients with HE.
- In stable patients with HE whom have a Model for End-Stage Liver Disease (MELD) score below 11, cirrhosis, and recurrent or persistent HE, obliteration of accessible portal-systemic shunts can be considered.
- Use of vegetable and dairy protein in place of animal protein can be considered in patients with recurrent/persistent HE.
  - Overall protein intake should not be compromised, and the patient's tolerance to the change must be considered.
- Liver transplantation should be assessed in patients with end-stage liver disease and recurrent or persistent HE that are not responding to other treatments.

    - Liver transplantation should be considered as soon as possible in patients with hepatic myelopathy, since there is no other therapeutic option.
- Dopaminergic treatment should be tested in patients with cirrhosis-related Parkinsonism.
- Fecal microbiota transplantation (FMT) is not a traditional treatment option for patients with recurrent/persistent HE but may be considered in light of validation in recent large clinical trials.
- Anti-HE treatment should be considered for patients with covert HE, for differential diagnosis and to prevent overt HE.
- Patients should be provided with information about driving safety, including potential risks with vehicle driving and overt HE episodes.
- Patients scheduled for non-urgent TIPS should be thoroughly assessed for the presence or history of HE.
    - One single episode of HE, especially if precipitated by bleeding, is not an absolute contraindication for TIPS.

Reference
European Association for the Study of Liver. (2022). EASL clinical practice guidelines on the management of hepatic encephalopathy. *Journal of Hepatology, 77*(3), 807-824. https://doi.org/10.1016/j.jhep.2022.06.001