STEPWISE PRACTICAL APPROACH TO A PATIENT WITH HEPATIC ENCEPHALOPATHY:

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STEP1: Define hepatic encephalopathy:

The West Haven criteria of altered mental state in HE (numerous studies have employed variations of these criteria).

Stage 0. Lack of detectable changes in personality or behavior. Asterixis absent.

Stage 1. Trivial lack of awareness. Shortened attention span. Impaired addition or subtraction. Hypersomnia, insomnia, or inversion of sleep pattern. Euphoria or Depression. Asterixis can be detected.

Stage 2. Lethargy or apathy. Disorientation. Inappropriate behavior. Slurred speech. Obvious Asterixis.

Stage 3. Gross disorientation. Bizarre behavior. Semistupor to stupor. Asterixis generally absent.

Stage 4. Coma.

STEP 2: CLASSIFY HEPATIC ENCEPHALOPATHY:

Type A	Encephalopathy from acute liver failure
Type B	Encephalopathy caused by portosystemic shunting, without intrinsic liver disease
Type C	Encephalopathy of cirrhosis associated with portosystemic shunting: Episodic: precipitated, spontaneous, or recurrent Resistant: mild, severe, treatment-dependent Minimal: previously known as ‘‘subclinical’’

Step 3: Treatment of underlying precipitating factor.

1]Dehydration

- causes includes excessive diuresis, diarrhea, or vomiting,
  Patients with severe ascites may be intravascularly depleted and dehydrated.
- Clinical signs of dehydration, and elevated serum creatinine and other laboratory tests consistent with hemoconcentration, establish the diagnosis.
- Treatment of Dehydration is reversed by discontinuation of diuretics, intravenous infusion of physiologic saline, and therapy for the underlying cause of increased fluid and electrolyte losses.

2} **Gastrointestinal bleeding** is identified and treated appropriately

3} Microorganisms cultured from infected sites (spontaneous bacterial peritonitis, urinary tract infection, pneumonia, cellulitis, and so forth) should be diagnosed and treated with appropriate antibiotics. **Broad-spectrum antibiotics** should be initiated after obtaining pancultures when infection is suspected in patients with stage III or IV HE, such as in patients with fever or unexplained leukocytosis.

4} **Hypokalemia** should be vigorously corrected with parenteral potassium in HE.

Mechanism: - as less potassium reaches the collecting tubules, more hydrogen ions are moved into the cells, leading to a state of relative intracellular acidosis. The kidneys then generate more ammonia and bicarbonate from glutamine in an effort to balance the acid-base status of the patient. This compensatory mechanism can worsen the HE

5} **Severe hyponatremia** (serum sodium! 125 mEq/L) can contribute to HE, particularly when the sodium level is less than 120 mEq/L.

- Discontinuation of diuretics and appropriate free-water restriction are required.
- Limited infusions of hypertonic saline (3% NaCl, 150 mL intravenous) may be needed for very severe hyponatremia.
- The new vasopressin receptor antagonists have shown promising results in treating severe hyponatremia with cirrhosis. They can be considered for patients with severe HE and severe hyponatremia

STEP 4} GENERAL CARE OF PATIENTS WITH HEPATIC ENCEPHALOPATHY:

patient should be nursed in icu

Continuous monitoring of vitals is mandatory.

Level of consciousness should be checked regular intervals by GCS SCALE

Head elevation up to 30 degree, maintain neutral neck position, avoid or minimize painful stimuli, hyperventilation to maintain PCO2 between 30-35 mm Hg, control of arterial hypertension, mannitol infusion and avoid fluid overload.
avoid agents that may exacerbate HE,
agents initiated at low doses and intermittently

- benzodiazepines - midazolam
- opiates - fentanyl, remifentanil

Mechanical ventilation may be needed for rapidly changing sensorium , or grade 3 & 4 HE, or for the respiratory distress, or child requiring high sedation.

Regular renal function and electrolye check should be done along with acid base status.

Patients with acute (fulminant) liver failure who develop stage III or IV HE have high frequency of significant cerebral edema with an attendant risk of uncal herniation, these patients are candidates for the placement of an intracranial pressure transducer. Complication like hemorrhage should be watched for.
The goal is to maintain ICP less than 20 mm of Hg and cerebral perfusion pressure (CPP) of > 50 to 60 mm Hg at all times

Mannitol, an osmotic diuretic, remains the mainstay of treatment for increased ICP. Mannitol should be administered when ICP >25 mm Hg for >10 mins, after the validity of the ICP calibration is confirmed. It has been shown to improve survival. A rapid bolus of 0.5 -1 g/kg as a 20% solution over a 15-min period is recommended, and the dose can be repeated if the serum osmolarity is less than 320 mOsm/l . There is no role for mannitol if serum osmolality is more than 320 mOsm/ liter. Serum osmolality should be assessed every 6 hrs, and mannitol boluses may be repeated if ICP remains >25 mm Hg and serum osmolality >320 mOsm/L.

hypertonic saline can be used in place of mannitol with maintaining serum osmolality < 360 mOsm/l . dose is 6 -8 ml /kg followed by 0.5 – 1 ml /kg/hr

Sodium thiopental can be used in controlling mannitol resistant cerebral oedema, giving a bolus dose of 2–4 mg/kg over 15 min followed by a slow intravenous infusion of between 1 and 2 mg/kg/hr.

Phenytoin (20 mg/kg bolus followed by 5mg/kg in two divided doses) infusion led to a significant reduction in seizure activity in adult patients

Hypothermia (core temperature of 32o C) has been shown to be effective in the management of severe intracranial hypertension, with a lowering of ICP and an improvement in CPP in adults
- Regular blood sugar monitoring is mandatory and frequently by finger stick (e.g. every 1–2 hrs).Intravenous glucose infusion (1.5–2.0 g/kg per day or 8 – 10 mg/kg/ min) is recommended inpatients who develop hypoglycemia. Insulin infusions may be used to maintain blood glucose levels <150 mg/dL, while also strictly avoiding hypoglycemia

renal failure is also addressed. Etiology varies as hepatorenal, ATN, Dehydration due to diuretics use, or nephrotoxic drugs.

Renal replacement therapies (HD, PD, CVVH,) can be considered as per need to maintain the fluid balance and nutrition .
LACTULOSE /LACTITOL :0.5 ml /kg/dose to maximum of 30ml /dose PO four times daily titrated to 3- 4 loose stool/day.
Lactulose enemas can be given as 20 % lactulose solution in 1-2 l of isotonic saline.

Rifaximin has gained rapid acceptance as either first-line or as adjunct therapy to lactulose. Rifaximin has a preferential site of action in the small bowel (presumably due to its enhanced solubility in bile) where it typically lowers the bacterial load 100–1,000-fold;
dose is 550 mg twice a day in adults.,10 mg / kg /dose in peds.
UNPROVEN DRUGS:
Sodium Benzoate and Sodium Phenylacetate**,**Ornithine-aspartate {LOLA},Use of BCCA INFUSION,ACARBOSE**,**ZINC **,**MELATONIN, L-Ornithine phenylacetate (LOPA), also known as OCR-002, A compound called AST-120 (Ocera Therapeutics)

STEP 5} NUTRITION IN HEPATIC ENCEPHALOPATHY:

There is no good clinical evidence supporting protein restriction in patients with acute hepatic encephalopathy

- Enteral nutrition should be administered whenever possible, with higher caloric density feeds preferred to avoid excessive free water and hypo-osmolality, which may exacerbate cerebral edema.

-Patients with grade III to IV hepatic encephalopathy usually do not receive oral nutrition. As soon as they improve, a general diet can be given.

-Dietary BCAA supplementation is indicated only in severely protein-intolerant patients. The benefits of BCAA (valine, leucine, and isoleucine) are believed to be 2-fold: They are essential

for protein production, and they are critical for the prevention of catabolism, which can worsen HE.

-There are insufficient data to recommend the use of branched chain amino acids (L Aspartate , LOrnithine i.e Hepamerz)

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