Hepatic Encephalopathy Protocol

Authors: Timothy Halterman, MD, and Robert Gish, MD

PURPOSE:

The following guideline outlines the recommended management of hepatic encephalopathy (HE). This is meant to be a general guidance document and clinical circumstances and the treatment of each patient will be evaluated on a case by case basis.

CLASSIFICATION:

Attempt to classify based on the type of underlying problem, disease severity, time course, and onset.

<table>
<thead>
<tr>
<th>Type</th>
<th>Grade</th>
<th>Time course</th>
<th>Spontaneous/precipitated</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (acute liver failure)</td>
<td>MHE</td>
<td>Covert</td>
<td>Spontaneous (no precipitating factor found)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Episodic (one episode in 6 months)</td>
<td></td>
</tr>
<tr>
<td>B (porto-systemic bypass)</td>
<td>2</td>
<td>Overt</td>
<td>Precipitated</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Recurrent (&gt;1 episode in 6 months)</td>
<td></td>
</tr>
<tr>
<td>C (cirrhosis)</td>
<td>4</td>
<td>Persistent (never returned to baseline)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Modified Axes of Hepatic Encephalopathy. Adapted from Viirstrup et al 2014 with permission.

West Haven criteria for disease severity

West Haven Criteria Used to Grade HE Severity

- Grade 0
  - Lack of detectable changes in personality or behavior
  - No asterix

- Grade 1
  - Trivial lack of awareness, shortened attention span, sleep disturbance, altered mood
  - Asterix may be present

- Grade 2
  - Lethargy, disorientation to time, amnesia of recent events, impaired simple computations, inappropiate behavior, slurred speech
  - Asterix is present

- Grade 3
  - Somnolence, confusion, disorientation to place, bizarre behavior, clonus, nystagmus, and positive Babinski sign
  - Asterix is usually absent

- Grade 4
  - Coma; unresponsive to verbal or noxious stimuli

DIAGNOSIS:

Based on composite clinical acumen as each case can vary but findings can include:

1. Motor system abnormalities including asterixis, hyperreflexia, hypertonia, bradykinesia, rigidity, tremors, ataxia, changes in hand writing. Take a complete history of any falls.
2. Behavioral or cognitive mental status changes including aggression, agitation, disorientation, personality changes, slurred speech, lethargic, apathetic, memory changes.
3. Sleep disturbances with altered sleep-wake cycles.
4. Impaired psychometric testing in those with covert hepatic encephalopathy.

Ammonia levels, if normal, can help rule out hepatic encephalopathy in a cirrhotic patient who appears normal on physical exam. However, elevated levels do not correlate with hepatic encephalopathy status or severity and should not be used alone without global assessment of patient to guide therapy. It is not advisable to check ammonia levels daily. Patients can be in a deep HE liver coma with “normal” ammonia levels. In summary ammonia testing is a poor tool to assess HE.

MANAGEMENT:

Assess for possible precipitating factors of hepatic encephalopathy:

1. Electrolyte abnormalities. All electrolytes, especially sodium and potassium, should be adequately repleted or corrected.
2. Infection. Evaluation for infection should include diagnostic paracentesis if ascites present, blood cultures, urinalysis/urine culture and chest X-ray. Evaluate teeth, prostate and sinuses.
3. GI bleeding, occult or overt.
5. Constipation.
6. Other forms of liver injury including alcohol induced, PV thrombosis, HCC.
7. Drugs including narcotics and benzodiazepines.

Rule out alternative etiologies such as CVAs, other metabolic encephalopathies. Consider a head CT scan if definitive diagnosis of hepatic encephalopathy is in doubt.

Inpatient treatment strategies:

1. Start Xifaxan 550 mg twice daily and lactulose 30-60 mL every 2-3 hours until BM and then every 6-8 hours to maintain 3-4 BMs per day or 750-1000mL (care to avoid >1L stool per day) per day of stool.
   a. If unable to tolerate lactulose orally, place nasogastric tube and begin lactulose via NG tube.
      i. Alternatively, use polyethylene glycol which may be less toxic to intestinal organs and cause less ileus via NG tube and titrate dose to produce 3 BMs or 750mL stool per day.
   b. If evidence of ileus, change lactulose to lactulose enemas, 300 mL lactulose mixed with 700 mL water. Administer every 4-6 hours depending on severity of encephalopathy.
2. Add zinc 220 mg daily to those who are zinc deficient or who do not respond to initial therapy.
3. If patient has persistent grade 2 encephalopathy despite above treatments, then add sodium benzoate 2 grams PO twice daily and increase to maximum 5 grams PO twice daily. This can be added to 7 up or coca cola to provide a buffer and lessen GI side effects or place down a...
feeding tube. Premedicate with sucralfate 1 gram 30 minutes prior to administering sodium benzoate to reduce nausea and vomiting.

4. If no improvement with treatment, need to assess for refractory etiologies including progressive liver disease, failure to identify infection or dehydration, ileus, long acting sedative drugs, concomitant central nervous system diseases or metabolic diseases (ie hypothyroidism), TIPS dysfunction, or spontaneous portosystemic shunts

5. Never use neomycin due to risk of otic- and nephron-toxicity

6. Probiotics in form of VSL #3 twice daily can be used in the hospital setting as adjunctive treatment.

Outpatient/Discharge treatment strategies:

1. Lactulose titrated to 2 BMs per day, typically around 20 grams/30 mL twice daily OR Xifaxan 550 mg twice daily if intolerant to lactulose

2. If >2 episodes of overt encephalopathy, recommend combination lactulose plus Xifaxan

3. VSL #3 probiotic twice daily can be used in those intolerant to lactulose. These have been shown to possibly be equivalent to lactulose

4. Polyethylene glycol or Miralax can be used in addition to lactulose in order to lower the dose of lactulose needed to produce 2 BM per day and lessen the side effects from lactulose

5. Should be advised to avoid excess red meat but not advised to limit protein consumption