Hepatic Encephalopathy
The case of T.L.
Michelle Hyman, Dietetic Intern
Good Samaritan Hospital
What is Hepatic Encephalopathy (HE)?

- A syndrome characterized by impaired mentation, neuromuscular disturbances, and altered consciousness.
- Occurs in patients with liver disease, especially cirrhosis.
Precipitating Factors

- GI bleeding
- Infection
- Electrolyte abnormalities
- Hyper/hypoglycemia
- Alcohol withdrawal
- Constipation
- Dehydration
- Portosystemic shunts
- Renal failure
Possible Mechanisms of HE

- Ammonia is considered an important etiologic factor.
- When the liver fails, it is unable to detoxify ammonia to urea.
- Ammonia is a direct cerebral toxin.
- Treatment is based on ammonia levels
Altered Neurotransmitter Theory

- A plasma amino acid imbalance exists in ESLD where BCAA (valine, leucine, isoleucine are ↓) and AAA (tryptophan, phenylalanine, tyrosine, methionine, glutamine, asparagine, histidine are ↑).

- May contribute to the development of HE

- AAA may limit the cerebral uptake of BCAA because they compete for carrier-mediated transport at blood-brain barrier
# Signs/symptoms

<table>
<thead>
<tr>
<th>Mental</th>
<th>Physical</th>
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</table>
| ❖ Forgetfulness  
❖ Confusion  
❖ Disorientation to time/place  
❖ Inappropriate behavior  
❖ Personality changes  
❖ Irritability | ❖ Sweet or musty odor breath  
❖ Change in sleep patterns  
❖ Slurred speech  
❖ Slowed/sluggish movement  
❖ Difficulty writing/drawing simple diagrams  
❖ Involuntary, jerky movement of hands |
Prevalence of HE

- Estimated to occur in 30-45% of patients with liver cirrhosis and 25-50% of patients with portosystemic shunts.

- 50-80% of patients with chronic hepatic failure
Prognosis

- Acute HE may be reversible.
- Chronic HE often continues to get worse/comes back.
- Both acute and chronic HE may \( \rightarrow \) irreversible coma and death.
- \( \sim 80\% \) die if they go into a coma.
- Recovery and the risk of the condition returning vary.
## The 4 Stages of HE (West Haven Scale)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Mild confusion, agitation, irritability, sleep disturbance, ↓ attention</td>
</tr>
<tr>
<td>II</td>
<td>Lethargy, disorientation, inappropriate behavior</td>
</tr>
<tr>
<td>III</td>
<td>Somnolent but arousable, incomprehensible speech, confused, aggressive behavior when awake</td>
</tr>
<tr>
<td>IV</td>
<td>★ Coma</td>
</tr>
</tbody>
</table>

(Hasse & Matarese, 2008, pp. 723)
HE Treatment

- Most patients show clinical signs of improvement of symptoms within 24-48 h of initiation of tx.

- Treat underlying cause.


- Antibiotics including rifaximin, neomycin.
Background Information

- Initials: T.L.
- Age: 67 years old
- Gender: Male
- Date of present admission: 3/12/12
- Date of discharge: 3/19/12
- Admitting diagnosis: HE
Psychosocial History

- Occupation: Nursing Home resident
- Marital status: Married
- Children: 1
- Socioeconomic status: unknown
- Nationality: White
- Social problems/handicaps: \( \not\exists \) known
- Habits: No h/o smoking. + history of ETOH abuse
Present Medical Problems

- T.L. was sent to Good Samaritan Emergency Department on 3/12 from nursing home 2° ↑ lethargy and inability to follow commands.

- Pt was noted to be non-verbal, non-responsive to stimuli (except painful) at ED

- Considered to be in coma (stage IV HE), likely 2° e.coli UTI
Previous illnesses/hospitalizations

- T.L. recently admitted to Good Samaritan Hospital with admitting dx of HE (2/2012).
- H/o prior episodes of HE requiring hospitalization.
- Past medical history: DM (has since been r/o), etoh abuse, un-resectable liver CA (hepatocellular carcinoma), HTN, cirrhosis, GI bleed
Nutrition Implications

- Protein restriction is controversial.
  - Exogenous protein is a source of ammonia
  - Dietary PRO →↑ in ammonia levels → HE?
  - Not proven in studies

- Benefit of supplements enriched with BCAA and restricted in AAA?

- Theory that vegetable proteins and casein may improve mental status compared with meat protein?
Protein and HE

- Previously, treatment of HE included ↓PRO diet (0-40 g/d)

- Recent studies suggest ↑protein
  - PRO restriction does not affect HE grade and can worsen nutritional status

- New consensus: avoid PRO restriction except for pts with severe PRO intolerance
  - Particularly patients with Grade III-IV HE, PRO may be restricted for short periods of time only.
# Newer Nutrition Recommendations of HE (in ESLF)

<p>| | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>Energy</strong></td>
<td>30-35-40 kcal/d</td>
</tr>
<tr>
<td><strong>Protein</strong></td>
<td>1.2-1.5 g/kg/d</td>
</tr>
<tr>
<td><strong>BCAA</strong></td>
<td>In severely protein-intolerant individuals</td>
</tr>
<tr>
<td><strong>Vitamins</strong></td>
<td>mvi</td>
</tr>
<tr>
<td><strong>Probiotics, prebiotics</strong></td>
<td>ing use for ammonia lowering and anti-inflammatory actions</td>
</tr>
<tr>
<td><strong>Fats</strong></td>
<td>30-35% of kcal. Use MCT if needed. *Escott-Stump</td>
</tr>
</tbody>
</table>

Bemeur, Desjardins, Butterworth, 2010. Review of nutrition in management of hepatic encephaloptahy in end-stage liver failure
Nutrition Recommendations

American College of Gastroenterology (Biel & Cordoba, 2009)

- Chronic encephalopathy: Focus protein intake on dairy products and vegetable-based diets. Consider oral BCAA if intolerant of all PRO.

- With coma: Use 0.5-0.6 g/kg; advance to 1-1.5 g/kg. Higher intake of BCAA of questionable benefit.

- For non-comatose patients, diet should provide moderate to high levels of PRO (d/c PRO restriction in most cases).

- Adequate intake of fluid/electrolytes.

- May need to restrict Na.

- Dietary intake must be adjusted according to changing status of pt.
Use of BCAA

- Pts with cirrhosis receiving BCAA may be more likely to recover from HE/may ↓ length of hospital stay in
- Use limited by poor availability, pt acceptance, cost.
- Controversial
Vegetable Protein

- May be better tolerated by pts with cirrhosis than meat-based PRO- not fully supported by literature.

- Theory:
  - $\uparrow$ fiber content $\rightarrow$ $\uparrow$ intestinal transit time and enhances intestinal nitrogen clearance.
  - $\downarrow$ colonic pH, prevents ammonia from being absorbed in the gut.
Objectives of Nutrition Care for HE

- Avoid skeletal muscle catabolism from inadequate oral intake, severely restricted diets or NPO status.

- ↓ ammonia and toxin production.

- Avoid daytime or nocturnal fasting by using frequent meals/evening snacks.

- Correct anemia, zinc, other deficiencies, (such as Mg, thiamin, folate)

- Improve quality of life.
T.L.’s Treatment

- Surgical: ∅

- Drugs:
  - Lactulose; Laxative used to treat ↑ ammonia levels
  - Rifaximin: Antibiotic
# T.L. Lab Values

<table>
<thead>
<tr>
<th>Lab</th>
<th>3/12/12</th>
<th>3/14/12</th>
<th>3/15/12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>110↑</td>
<td>111↑</td>
<td>122↑</td>
</tr>
<tr>
<td>BUN</td>
<td>20↑</td>
<td>19↑</td>
<td>13</td>
</tr>
<tr>
<td>Creat</td>
<td>1.1</td>
<td>1.4↑</td>
<td>1.5↑</td>
</tr>
<tr>
<td>Sodium</td>
<td>140</td>
<td>142</td>
<td>148↑</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.4</td>
<td>4.1</td>
<td>3.5</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.7↘</td>
<td>2.5↘</td>
<td>-----</td>
</tr>
</tbody>
</table>
# T.L. Liver Function Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>3/13</th>
<th>3/14</th>
<th>3/15</th>
<th>Acceptable Ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ammonia</td>
<td>141↑</td>
<td>158↑</td>
<td>58↑</td>
<td>7-27 µmol/dL</td>
</tr>
<tr>
<td>ALT</td>
<td></td>
<td>93↑</td>
<td></td>
<td>4-40 U/L</td>
</tr>
<tr>
<td>AST</td>
<td></td>
<td>90↑</td>
<td></td>
<td>10-37 U/L</td>
</tr>
<tr>
<td>GGT</td>
<td></td>
<td>378↑</td>
<td></td>
<td>7-51 U/L</td>
</tr>
<tr>
<td>LDH</td>
<td></td>
<td>322↑</td>
<td></td>
<td>105-230 U/L</td>
</tr>
<tr>
<td>Lipase</td>
<td></td>
<td>344</td>
<td></td>
<td>16-63 U/L</td>
</tr>
<tr>
<td>Alk Phos</td>
<td></td>
<td>293↑</td>
<td></td>
<td>40-120 U/L</td>
</tr>
<tr>
<td><strong>Medication</strong></td>
<td><strong>Indication</strong></td>
<td><strong>Side effects</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>---------------</td>
<td>------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactulose ★</td>
<td>Laxative-to treat ↑ ammonia levels</td>
<td>N/v, cramps, diarrhea, flatulence. ↑ glucose, ↓ NH3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aldactone</td>
<td>Antihypertensive, diuretic</td>
<td>Anorexia, ↓ wt, ↑ thirst, dehydration, n/v, diarrhea, dry mouth ↑ K+, ↓ Na, ↓ Cl, ↑ BUN, ↑ Creat, ↑ Mg, ↑ LDL, ↓ HDL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lasix</td>
<td>Diuretic (K-depleting), antihypertensive</td>
<td>Anorexia, ↑ thirst, n/v, diarrhea, constipation. ↓ K, ↓ Mg, ↓ Na, ↓ Cl, ↓ Ca, ↑ glu, ↑ BUN, ↑ creat, anemia, ↑ Chol, ↑ LDL, ↑ TG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nadolol</td>
<td>Anti-hypertensive</td>
<td>No pertinent side effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vit B1, KCl, mvi</td>
<td>Anti-hypertensive</td>
<td>No pertinent side effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifaxamin ★</td>
<td>Antibiotic</td>
<td>No pertinent side effects</td>
<td></td>
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</tr>
</tbody>
</table>
Previous Diet Order/Nutrition History

- At nursing home, L.D. was receiving NAS diet, regular consistency, with thin liquids.

- At Good Samaritan Hospital (during previous admission) pt was receiving 2 g Na diet.
Anthropometrics

- Height: 72.8”
- Weight: 191# (86.8 kg) per nsg assessment
- UBW: 197# (on 2/25/12)
- ↓ 6# x 3 weeks (3.0% loss)
- 96.9% UBW
- IBW: 178# ±10%
- %IBW: 107%
- BMI: 25.3
Assessment of T.L.’s Nutrient Needs

- 3/14: Initial nutrition assessment completed

- Initial estimates of T.L.’s current nutrition needs:
  - 2170 kcal (based on 25 kcal/kg)
  - 69 g PRO (based on 0.8 g/kg)
  - Fluid needs: per MD management (MD order for fluids)

- 3/14, SLP unable to perform swallow evaluation 2° pt’s lethargy.
T.L. Diet Order

- 3/12: NPO
- 3/13-3/14: Jevity (1.2 kcal) via NGT 30 mL/hr continuous (per MD order)
- Current TF provides:
  - 864 kcal (40% of estimated kcal needs)
  - 40 g pro (58% of estimated PRO needs)
  - 581 mL fluid
Nutrition Diagnosis

- **Problem**: Less than optimal enteral nutrition (NI- 2.5) related to current TF volume/formula as evidenced by current TF providing < estimated kcal and protein needs.

- **Goal**: Pt will receive and tolerate ≥75% of estimated nutrient needs via TF within 48 hours.

- **Interventions**:
  1. Recommend change TF to Nutrihep (start at 30 mL/hr, ↑15 mL Q 8° until goal rate of 65 mL/hr is met)
     - At goal rate, would provide 2340 kcal, 62 g PRO, 1185 mL fluid
  2. Monitor for re-try of SLP evaluation.
  3. Adjust TF as medical status changes.
What is Nutrihep?

- A TF formula high in BCAA and low in AAA.
- Suitable for lactose intolerance, gluten-free, low residue.
- Indications for use: HE, malnutrition, individuals with galactosemia
- Protein source: Crystalline L-amino acids, whey protein concentrate
- Fat source: MCTs (coconut, palm kernel oil), corn oil
**Nutrihep-Nutrition Information (1L)**

<table>
<thead>
<tr>
<th></th>
<th>1.5/mL</th>
<th>(1500 kcal/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cal/mL</td>
<td>1.5/mL</td>
<td>(1500 kcal/L)</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>290</td>
<td></td>
</tr>
<tr>
<td>Fat (g)</td>
<td>21.2</td>
<td></td>
</tr>
<tr>
<td>Water (g)</td>
<td>760</td>
<td></td>
</tr>
<tr>
<td>To meet 100% RDIs</td>
<td>1000 mL</td>
<td></td>
</tr>
<tr>
<td>Sodium (mg)</td>
<td>160</td>
<td></td>
</tr>
<tr>
<td>Potassium (mg)</td>
<td>1320</td>
<td></td>
</tr>
</tbody>
</table>
3/15: Update on T.L.’s Status

- Passed SLP evaluation
  - SLP recommended to initiate p.o. diet, c chopped consistency and regular, thin liquids. Set-up help.

- MD order to d/c NG tube
  - Pt. had already pulled out the NG tube

- MD order for mechanical chopped diet, 2 g Na
3/16: Informal Follow Up with T.L.

- T.L.'s complaints of n/v, constipation, diarrhea, or problems chewing or swallowing.

- Still receiving set-up help with meals, although requiring less assistance per nsg.

- Still without his dentures.

- Lunch:
  - 4 oz milk, 4 oz apple juice, ¼ macaroni and cheese, 4 oz green beans
    - ~360 kcal, 13 g PRO

- Plan: Full re-assessment due on 3/19
Summary

- Although T.L. had a fast recovery, his admitting condition was poor.
- In some cases, HE can be fatal, or it can have permanent adverse medical effects.
- HE can also become recurrent, as seen with this case.
- Treatment regarding nutrition for HE is controversial.
  - Current guidelines: treat HE with medications, not PRO restriction.
  - PRO does not exacerbate HE and can improve outcomes.
  - Severe HE: temporary PRO modification/restriction can be considered.

- Cirrhotic pts with HE

- Group A (n=10): low PRO-
  - Day 1-3: 0 g PRO
  - ↑ progressively q 3 days (12, 24, 48 g) until 1.2 g/kg/d was reached

- Group B (n=10): normal PRO- 1.2 g/kg/d from start

- NTR via NGT for 2 weeks, continuous (30 kcal/kg/d)

- Conclusions:
  - No major benefit of PRO restriction
  - Low PRO diet in short term did not affect plasma ammonia or liver function. Had ↑ PRO breakdown.
  - Pts with episodic HE can safely tolerate normal PRO diet
  - Lack of difference between starting normal PRO vs. progressive ↑ing pro intake indicates PRO tolerance is higher than previously thought
References


References, continued


