Change in Mental Status
Hepatic Encephalopathy (HE)

Management Overview
Mrs. Johnson in room 113 just had a fall with no injuries. Sorry to wake you at 4:30am but we needed to report it. Your 82 year old patient had a change in mental status all day.
Do you want a U/A and anything else?
Causes of Altered Mental Status in Adults

- Fever or infection
- Poisoning or overdose
- Blood sugar/endocrine problems
- Head injury
- Inadequate oxygenation or ventilation
- Conditions leading to decreased blood flow or oxygen to the brain
- Cardiac or diabetic emergencies
- Shock
- Stroke
- Behavioral Illness
- Seizures
Behavior / Personality Changes

- Increased fidgeting
- Change in cooperation
- Difficulty in attention
- Change in task segmentation ability
- Focus fluctuation
- Orientation fluctuation
- Liver Flap
- Delirium symptoms
- Sleep cycle alteration-night-day confusion
- Calling out, making sounds, moaning
- Less interest in surroundings
- Change in verbalization
- Change in socialization
- Withdrawal from activities or meals
- Altered ability to dress, eat or participate in activities of daily living
- May seem intentionally obstinate
- Unusual agitation
- Combativeness
Level of Consciousness and Awareness

- Bizarre behaviors, extremely different actions for this resident
- Alteration in consciousness
- Glasgow coma definitions
- Westhaven Criteria
- Significant cognitive changes
- Withdrawal and inactivity and minimal engagement
- Coma
- Shifting attention
- Combativeness
Prevalence
Chronic Liver Disease (CLD) affects over 5.5 million patients in the USA\textsuperscript{1}, of whom more than 600,000 have cirrhosis.\textsuperscript{2}
Hepatic Encephalopathy (HE)

HE is most commonly a syndrome observed in patients with cirrhosis.

Subtle signs of it are observed in nearly 70% of these patients. Given its extremely high prevalence, HE should be a condition that LTC providers are readily able to diagnosis and treat. However, due to its episodic nature, slow progression and symptoms which overlap those of other diseases, clinicians often miss this diagnosis.

Top cause of 30-day hospital readmissions

LTC providers need to be both knowledgeable and vigilant regarding its prevalence, pathophysiology, diagnosis and treatment.

3. Elwir 2017
Diagnosis
Cirrhosis

Ammonia

Bacterial translocation

Activation of systemic inflammatory cells

Brain pathogen recognition receptors

Immune failure

Inflammation

Brain inflammation
- Astrocytes
- Glial cells

Endothelial dysfunction
- iNOS
- eNOS dysfunction
- Adhesion molecules

Infection
- Cytokines
- Oxidative stress
- Prostaglandins
- Activation of Transcription Factors

T cell

Macrophage

B cell

Reduced Gut Motility

Increased gut permeability; bacterial translocation

Bacteria overgrowth in gut lumen

Cerebral Edema

Hepatic Encephalopathy

5 Jalan 2010.
Diagnosis and Factors

Diagnosis of hepatic encephalopathy
• Elevated free arterial serum arterial ammonia level. **BUT NOT ALWAYS**…
• EEG: shows non-specific high amplitude low frequency waves and tri-phasic waves.
• CT scan and MRI of the brain may be necessary in ruling out intracranial lesions. In acute encephalopathy brain edema may be seen.

Common precipitating factors:
Dehydration, ascites, changes in diet and alcohol use

Others include: Renal failure, GIT bleeding, infection, constipation, increased dietary protein intake. Opiates, benzodiazepines, anti-depressants and anti-psychotics may also worsen encephalopathy. Hypokalemia and alkalosis (due to vomiting or excessive use of K-losing diuretics) increase solubility of NH3 thus increase its passage across the blood brain barrier.

Differential diagnosis of encephalopathy (other causes of coma):
Intracranial lesions (intracranial he, tumor, abscess), infections (meningitis, encephalitis), metabolic encephalopathy (hypoglycemia, uremia, electrolyte imbalance), alcoholic encephalopathy, post-seizure encephalopathy.
ASTERIXIS is a tremor of the hands when the arms are extended and the hands are bent upward. It is associated with metabolic encephalopathies affecting diencephalic motor centers and presents as a “flapping” motion as the patient is unable to maintain dorsiflexion.

It is common in decompensated liver failure, but not in advanced cases and coma. It is also seen in carbon dioxide intoxication, uremia, organ failure, and stroke of basal ganglia.
Treatments
Mechanism of Action of Lactulose for OHE

- A non-absorbable disaccharide
- It produces osmosis of water — Diarrhea \(^6,^7\)
- It reduces pH of colonic content & thereby converts freely diffusible NH\(_3\) into ammonium ions (NH\(_4^+\)), which cannot be absorbed and are therefore excreted.\(^6,^7\)
- Lactulose reaches the colon unsplit. It is then converted by bacteria to organic acids and an acid stool results. This may also affect the ionization of ammonia in the colon and reduce its absorption.\(^6,^7\)
- The current AASLD/EASL guideline (2014) recommends rifaximin as an add-on to lactulose for prevention of recurrent episodes of HE after the second episode.\(^8\)

\(^6\) Reena
\(^7\) Davidson’s
\(^8\) AASLD-EASL 2014
Rifaximin

Rifaximin is a minimally absorbed oral antimicrobial agent that is concentrated in the gastrointestinal tract, has broad-spectrum activity against gram+ and gram- aerobic and anaerobic enteric bacteria, and has a low risk of inducing bacterial resistance.\(^8\)

In randomized studies, rifaximin was more effective than non-absorbable disaccharides and had efficacy that was equivalent to or greater than that of other antibiotics used in the treatment of acute HE.\(^9\)

Note that rifaximin is not a treatment for OHE. It should rather be positioned as a secondary prophylaxis strategy for use with lactulose to prevent recurrence of HE and related hospitalizations.\(^{12}\)
Randomized, Double-Blind, Controlled Trial

XIFAXAN reduced the risk of OHE recurrence by 58% and HE Related hospitalizations by 50% versus Placebo.

91% of patients in both arms of the trial were on lactulose which means this data reflects benefits of rifaximin over and above those which previous studies have shown are due to lactulose alone.

This is important in weighing the value of managing patients with a regimen of lactulose alone, as compared to one with a combination of lactulose and rifaximin.
Usual Adult Dose for Hepatic Encephalopathy

Lactulose 30 mL orally 3 times a day or 300 mL in 700 mL water or normal saline as an enema retained for 30-60 minutes every 4 to 6 hours.

Maintenance dose: 30-45 mL orally 3x a day.

Rifaximin 550 mg orally twice a day
American Association of the Study of Liver Disease & European Association for the Study of the Liver (AASLD/EASL)

AASLD/EASL guidelines recommend combined lactulose plus rifaximin for prevention of HE after the second episode. 8

Rifaximin has excellent characteristics, including a slow rate of systemic absorption, a broad spectrum of antibiotic activity, and a low frequency of side effects. 12

This particular guideline on combination therapy is given the highest recommendation (Grade 1, A, 1) based on scientific merit and cost-effectiveness. 8,13
KTAP
Key Take Away Points
1. Keep HE (Hepatic Encephalopathy) top of mind as one potential cause for ‘Change in Mental Status.

2. Develop a process for your facility to efficiently and effectively diagnose and treat HE.

3. The AASLD/EASL guideline recommendations are a helpful resource for the management of HE in the LTC environment.

4. Combination therapy with lactulose and rifaximin following an episode of OHE has been well studied, and proven to reduce the risk of OHE recurrence and HE related hospitalizations.
References:


