Management of Hepatic Encephalopathy in Hospice and Palliative Care

ProCare HospiceCare Lunch and Learn Series

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Contact Hours – Nursing
1.0 Contact Hour

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Successful Completion Criteria

- *Register for the activity*
- *Complete and submit the sign in sheet*
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- *Complete and submit the participant evaluation*
- *Certificate will be emailed upon completion of the criteria*

Objectives

1. Define and describe hepatic encephalopathy
2. Summarize preferred treatment approach
3. Identify preferred pharmacotherapy
4. Explore three pertinent case studies

End-Stage Liver Disease

- Also known as chronic liver failure
- Liver damage progresses over months, years, or even decades
- Cirrhosis (scarring of liver tissue) is generally the final common end point
- Progression from compensated to decompensated cirrhosis occurs when serious complications occur
- Common complications include: ascites (most common), hepatic encephalopathy (HE), spontaneous bacterial peritonitis (SBP), and esophageal varices

Hepatic Encephalopathy (HE)

- Encephalopathy is a disease in which brain function is altered by an agent or condition, and so, hepatic encephalopathy is brain dysfunction as a result of hepatic dysfunction
- Develops in 30-45% of patients with decompensated cirrhosis
- Once the liver is unable to adequately filter toxins (namely, ammonia), these toxins build up in the body and eventually affect the brain
- This results in a complex neuropsychiatric syndrome marked by a constellation of personality and mental status changes, intellectual impairment, and altered level of consciousness
- Generally associated with a precipitating factor (alcohol binge, surgery, dehydration/ hypovolemia, electrolyte disturbance (such as hyponatremia or hypokalemia), metabolic acidosis, hypoxia, hypoglycemia, medication(s), GI bleed, infection, hepatocellular cancer, vascular occlusion, etc.)
- Diagnosis is by exclusion of other causes of encephalopathy, identification of precipitant(s), and successful empiric treatment (lack of response within 72h generally warrants further differential diagnoses)

Common Signs and Symptoms of HE

Mental	*Physical*
Confusion	Changes in sleep pattern
Shortened attention span	Difficulty with hand movements
Forgetfulness	Musty breath
Mood swings	Sweet breath
Personality changes	Slurred speech
Inappropriate behavior	Jumbled speech
Difficulty with basic arithmetic	Slowed movement
Anxiety	Sluggish movement
Fearfulness	Asterixis (shaking or flapping of hands or arms)
Disorientation	Coma

West-Haven Criteria (WHC) for HE

Overt hepatic encephalopathy (OHE) is diagnosed by clinical criteria and generally graded according to the WHC.

Minimal: Minimal Hepatic Encephalopathy (MHE), previously known as subclinical HE, minimal to no changes in memory, concentration, mental function, and coordination

Grade I: mild lack of awareness, shortened attention span, impaired ability to perform mental tasks (such as addition or subtraction), mild asterixis

Grade II: lethargy or apathy, minimal disorientation or inappropriate behavior, slurred speech and obvious asterixis

Grade III: somnolent but arousable, gross disorientation and bizarre behavior, muscular rigidity and clonus

Grade IV: coma (does not respond even to painful stimuli)

Preferred Treatment Approach

Step 1: Eliminate or manage underlying (precipitating) factors

Step 2: Nonpharmacological (lifestyle) interventions

Step 3: Pharmacotherapy and supportive care

Underlying Factors & Nonpharmacological Interventions

- Rule out broader causes of altered mental status and other types of encephalopathy
- Manage precipitating causes: *substance abuse including alcohol, trauma, tumor, dementia, mental health disorder, epilepsy, stroke, kidney disease, poisoning, anoxia, poor nutrition, hypovolemia (often diuretic-induced), GI bleeding, constipation, infection, etc.*
- Avoid medications that depress CNS activity, if possible, such as *opioids, benzodiazepines, antidepressants, antipsychotics, other sedatives, anticonvulsants, tacrolimus, and cyclosporine*
- Avoid protein overload *(specifically red meat)*

Case 1

Mrs. E.Z. is an 81-year-old woman with advancing dementia and a history of a recent hip fracture, liver mass (detected during hospitalization for the fracture), diabetes, and COPD. She is allergic to penicillin.

Current medications: donepezil 10mg po daily, memantine 10mg po daily, haloperidol 0.5mg po 4 times a day scheduled, morphine er 15mg po tid, morphine 20mg/ml 5-10mg po/sl q2h prn pain/sob, sliding scale insulin as directed, oxygen vnc as directed, multivitamin 1 tab po daily, and calcium 500mg po bid.

Pain is well controlled, but family reports increased lethargy and confusion (such as the patient not being able to add correctly or play cards), frequent napping throughout the day when nobody is around to talk to, fidgeting and taking oxygen mask off at night (when used to sleep through the night), and sleep cycle disturbances (days and nights mixed up). A family member read that these are hallmark signs of hepatic encephalopathy from liver cancer and would like to know what treatment would be recommended. When asked, the family reports that there is no tremor or "flapping" of hands or limbs.

Pharmacotherapy

- Lactulose is an osmotic non-absorable disaccharide laxative that also lowers the colonic pH. Due to its record of safety and efficacy in clinical practice, lactulose remains the mainstay of pharmacotherapy.
- Antimicrobials (neomycin, metronidazole, and vancomycin) reduce bacterial production of ammonia and other bacteria-derived toxins, but associated adverse effects have limited their use. However, serious adverse effects often take several months to develop and are not as much of a concern in hospice and palliative care (where patients have a prognosis of 6 months or less) as in standard practice. Neomycin is generally the preferred agent, but metronidazole or vancomycin may be considered if neomycin is inappropriate due to allergy or intolerance.
- Rifaximin is a novel antimicrobial agent (may restore microflora imbalance) and is generally considered as or more effective and better tolerated than the aforementioned agents. Despite less risk of serious adverse effects when compared to the other agents, rifaximin generally remains third line in hospice and palliative care due its extreme cost and limited data in patients with very end-stage liver disease.

Lactulose 10g/15ml Solution (Constulose, Enulose, Generlac, Kristalose)

- Generally first line
- Generally dosed starting at 30ml po bid and titrated to target 2-3 soft bm's per day or an acceptable dose to manage the patient's symptoms
- Overt HE episodes may also be treated with 30ml po q1-2h until at least 2 soft bm's are produced and then titrated to maintain 2-3 soft bm's per day as noted above
- May also be given pr (per rectum) in enema form
- Costs **~$5.00** per day

Neomycin 500mg Tablet (Mycifradin)

- Generally second line
- Add onto lactulose when lactulose is titrated and tolerated but ineffective (or use in place of lactulose when lactulose is not tolerated)
- Generally dosed at 1-2g per day in divided doses to manage chronic HE and 3-6g per day in divided doses for a 1-2 week period to manage acute HE
- Costs **~$8.00** per day (for conventional approach of 1g po tid)
- Poorly absorbed but sufficient exposure may result in ototoxicity and nephrotoxicity (long-term use generally requires annual auditory and renal function testing)

Rifaximin 550mg Tablet (Xifaxan)

- Generally third line
- Add onto lactulose or use instead of neomycin (or other antibiotic) when other feasible approaches have failed
- Generally dosed at 550mg po bid
- **Costs ~$85.00 per day**

Case 2

Mr. ET is a 56-year-old man with end-stage liver disease and a history of alcohol abuse, smoking, liver and biliary cirrhosis, and hypertension. He has nkda.

Current medications: ursodiol 250mg po bid, hydrochlorothiazide 25mg po daily, lorazepam 1mg po q4h prn anxiety/restlessness, and lactulose 10g/15ml 15ml po bid.

Mr. E.T. has recently been diagnosed with hepatic encephalopathy as other potential causes have been ruled out. Despite routinely taking lactulose as directed and reporting regular bowel movements, the mood swings and bouts of confusion and irritability associated with the encephalopathy are worsening, and the patient is only eating 1-2 small meals a day.

Case 3

Miss O.K. is a 62-year-old woman with end-stage liver disease and a history of obesity, HLD, OP, anemia, DM, NASH, and hepatic encephalopathy. She is allergic to penicillin and metronidazole.

Current medications: atorvastatin 10mg po qhs, Caltrate 600+D3 1 tab po bid, ferrous sulfate 325mg po bid, metformin 500mg po bid, insulin as directed, and lactulose 10g/15ml 45ml po bid.

Despite taking lactulose as directed and maintaining a diet rich in fiber, Miss O.K. is only having 1-2 bm's a day. Miss O.K. commented that she felt like she "lost her mind" last month in the hospital when she experienced hepatic encephalopathy and is requesting a stronger preventative care plan now that she is home alone.

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Thank You!

- *Question and answer session*
- *Final remarks*
- *Please send any additional questions to bgillis@procarerx.com*