Clinical Resource Guide:
Hepatic Encephalopathy

INTRODUCTION TO HEPATIC ENCEPHALOPATHY MANAGEMENT

Hepatic encephalopathy (HE) is a neurological disorder that occurs as a result of liver failure. In end-stage liver failure, the body's ability to remove toxins from the blood is impaired. This can result in the accumulation of ammonia in the brain, which is thought to be responsible for the symptoms experienced. Symptoms of hepatic encephalopathy can range from mild to confusion and disorientation to severe delirium and somnolence. Common causes of HE include cirrhosis, hepatocellular carcinoma, metastases to the liver, and acute liver failure. The purpose of this guide is to serve as a resource for the hospice care team to provide appropriate care to manage symptoms, provide comfort and support end-of-life care for patients with hepatic encephalopathy.

Pharmacist Corner Objectives

1. Identify causes exacerbating hepatic encephalopathy, and how to prevent/avoid
2. Classify the severity of hepatic encephalopathy experienced by the patient
3. Select the most efficacious, cost-effective medication for management of hepatic encephalopathy

FACTORS EXACERBATING HEPATIC ENCEPHALOPATHY IN CIRRHOTIC PATIENTS

CAUSES	SPECIFIC CONTRIBUTORS	
Medication	• Benzodiazepines • Opioids	• Hypnotics • Alcohol
Vascular occlusion	• Hepatic vein thrombosis	• Portal vein thrombosis
Dehydration	• Paracentesis • Vomiting	• Hemorrhage • Diarrhea
Increased ammonia production/absorption	• Excess protein intake • Hypokalemia • Metabolic acidosis	• GI bleed • Constipation • Infection

CLASSIFICATION OF HEPATIC ENCEPHALOPATHY SEVERITY

WEST HAVEN CLASSIFICATION SYSTEM	
GRADE 0	Minimal hepatic encephalopathy; lack of detectable changes in personality or behavior; minimal changes in memory, concentration, intellectual function, and coordination; asterixis is absent.
GRADE 1	Trivial lack of awareness; shortened attention span; impaired addition or subtraction; hypersomnia, insomnia, or inversion of sleep pattern; euphoria, depression, or irritability; mild confusion; slowing of ability to perform mental tasks.
GRADE 2	Lethargy or apathy; disorientation; inappropriate behavior; slurred speech; obvious asterixis; drowsiness, lethargy, gross deficits in ability to perform mental tasks, obvious personality changes, inappropriate behavior, and intermittent disorientation, usually regarding time.
GRADE 3	Somnolent but can be aroused; unable to per- form mental tasks; disorientation about time and place; marked confusion; amnesia; occasional fits of rage; present but incomprehensible speech.
GRADE 4	Coma with or without response to painful stimuli.

PHARMACOLOGIC MANAGEMENT OF HEPATIC ENCEPHALOPATHY

Therapy often starts with addressing correction of any underlying causes (noted above) if consistent with goals of care. Specific HE therapy is designed to limit production and increase excretion of ammonia and other GI toxins. Non-absorbable lactulose increases GI transit time and promotes bacterial fermentation, which negatively impacts ammonia producing bacteria.

MEDICATION	DOSE	DOSE ADJ.	ADVERSE EFFECTS	VS. PLACEBO	VS. LACTULOSE	COST/ DAY
Lactulose	15-45ml/dose 2-3 dose/day	no	excessively sweet taste, GI upset	Superior	n/a	15ml TID: $1.29 45ml TID: $3.87
Metronidazole	250-500mg BID	renal	GI upset, loss of appetite, diarrhea	not trialed	equivalent	250mg BID: $0.94 500mg BID: $0.90
Neomycin	500-1000mg BID-QID	no	Diarrhea, dyspnea, thirst	not trialed	equivalent	500mg QID: $100
Rifaximin	550mg BID-TID	no	Edema, nausea, dizziness, muscle spasms	Superior	equivalent	550mg BID-TID: $103-$155

ADVANCED CARE PLANNING AND SUPPORTIVE CARE

The patient's values, goals of care, and treatment options should be discussed in the context of the poor prognosis of HE. A health care representative should be established in patients with cirrhosis before cognitive impairment prevents this from happening without patient input.

Additionally, the family and the patient should be educated to help identify symptoms of HE, understand the fluctuating course of the disease, and avoid contributing causes whenever possible. Patients and families should also be counseled on the risks of driving with hepatic encephalopathy, as symptoms impairing cognition pose risk to patient and others. Finally, the risks of falls, skin breakdown and aspiration should be discussed with the patient and family to ensure appropriate understanding and to set expectations.

Establishing patient goals will help the patient and hospice team navigate the provision of care as the patient approaches the end, and ensure the best possible care is provided in accordance with patients desires.

References

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