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Primary Care Management of Hepatic Encephalopathy: A Common Cirrhosis Complication

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ABSTRACT

Hepatic encephalopathy develops in up to 50% of patients with cirrhosis and is associated with significant morbidity and mortality. Hepatic encephalopathy ranges of covert, or asymptomatic but with abnormal neuropsychometric studies, to overt, or presence of symptoms. Overt hepatic encephalopathy has a significant impact on quality of life and health care costs. The pathophysiology of hepatic encephalopathy is multifactorial and not well understood. There is a general consensus that ammonia and inflammation act synergistically, causing astrocyte swelling and cerebral edema. Increasing the nurse practitioner's knowledge about prevention and management of hepatic encephalopathy is important to improve health care outcomes.

Keywords: cirrhosis, covert, hepatic encephalopathy, overt

Chronic liver disease is the 12th leading cause of mortality in the United States.[1] Approximately 5.5 million people in the US have cirrhosis and have a 15% risk of having a hepatic encephalopathy (HE) episode.[2] Once HE occurs, the 1-year mortality is over 60%,[3] and it is associated with a poor prognosis.[4] Although potentially reversible, HE is a spectrum of neuropsychiatric abnormalities that range from normal cognitive function to coma.[3] Frequent hospitalizations are common and can cause a significant burden to the patient and family. In 2003, the US generated charges for HE hospitalizations alone to up to US $1 billion.[5]

Although liver transplantation (LT) is a curative option for patients with cirrhosis, the number of patients waiting for LT outweighs the number of available organs for transplantation. The prioritization of LT uses the Model for End-Stage Liver Disease (MELD) allocation process in an attempt to objectively identify the sickest patients. The MELD score incorporates the serum total bilirubin, creatinine levels, and international normalized ratio. The available organ is offered to the patient with the highest MELD score. HE is currently not factored in the MELD scoring system, and its severity, cost, and risk of mortality may be underestimated.[6] With the high mortality rate and high cost associated with HE, this article emphasizes the importance of prevention, appropriate treatment, and timely management.

PATHOPHYSIOLOGY

HE is a very complex process and is still not well understood.[7] The pathogenesis is believed to be related to the exposure of the brain to elevated amounts of neurotoxins, particularly ammonia and other gut-derived toxins, leading to astrocyte (brain cells) swelling and the development of neurochemical and neuroinflammatory changes.[8] Factors that can precipitate HE and increase the production of these toxins include infection, electrolyte imbalances, gastrointestinal bleeding, dehydration, anemia, and/or placement of a portosystemic shunt[1] (Table 1). In cases of hypokalemia with impaired renal function, there is reduced excretion of ammonia from the body. This can result in a buildup of ammonia in the systemic circulation and, ultimately, acidosis.

Table 1. Causes and Precipitants of Hepatic Encephalopathy[13]

Increased ammonia production, absorption, or entry into the brain
Infection
Excess dietary intake of protein
Gastrointestinal bleeding
Electrolyte disorder
Constipation
Metabolic alkalosis
Drugs
Benzodiazepines
Narcotics
Alcohol
Dehydration
Vomiting
Diarrhea
Hemorrhage
Diuretics
Large-volume paracentesis
Portosystemic shunting
Radiographic or surgically placed shunts
Spontaneous shunts
Vascular occlusion
Portal vein thrombosis
Hepatic vein thrombosis
Primary hepatocellular carcinoma

Dehydration, caused by high-dose diuretics or high-dose lactulose, can be another precipitating factor because of the increased concentration of ammonia. Because ammonia is a by-product of protein breakdown, conditions that increase the occurrence of protein breakdown can precipitate HE. Although the exact pathophysiology is unclear, accumulating data suggest that the cascade of neuropsychiatric sequelae of HE may have a long-term effect as well as a permanent negative impact on patients than originally suspected.[8] Recent research findings on post–liver transplant patients with a history of multiple bouts of HE showed that full reversibility of mental deficits is unlikely.[6]

GRADES AND CLASSIFICATIONS OF HE

The West Haven Criteria (WHC) is most often used to grade HE, with scores ranging from 0 to 4 (4 being coma). Because of the challenge of diagnosing patients with minimal HE, the guidelines from the International Society for Hepatic Encephalopathy (ISHEN) and Nitrogen Metabolism have combined the terms *minimal HE* and *grade 1 encephalopathy* and changed the name to *covert hepatic encephalopathy* (CHE).[3] CHE means that a mental defect has not been detected and/or there is no disorientation or physical symptoms. Overt hepatic encephalopathy (OHE), on the other hand, is categorized by WHC into grades 2 to 4. Grade 2 is characterized by lethargy, disorientation, and obvious asterixis (described later); grade 3 consists of somnolence with arousability, gross disorientation with bizarre behavior, and muscle rigidity with clonus and hyperreflexia; and grade 4 consists of coma with decerebrate posturing in patients with cirrhosis after the exclusion of neurologic or metabolic abnormalities.[9] Significant evidence supports that there is a continuum of neurologic impairment that is associated with CHE, and it strongly predicts the subsequent progression to HE[10] (Table 2).

CLINICAL FINDINGS OF HE

Patients with HE present with a variety of neuropsychiatric abnormalities ranging from abnormal sleep patterns, irritability, changes in personality/behavior, an impairments in attention, coordination, or mental function to neurologic symptoms with flapping tremors and/or coma (usually with a rapid progression).[11] Altered behavior with mood changes, irritability, and apathy may be reported by caregivers. As HE progresses, alterations in consciousness and motor function occur. Changes in sleep-wake cycle with excessive daytime sleepiness become more notable. Patients may develop disorientation to time, place, and person; agitation; stupor; somnolence; and, ultimately, coma. Neurologic symptoms can be observed such as hypertonia, hyperreflexia, and a positive Babinski sign. Other findings include slowness in speech, Parkinson-like tremors, muscular rigidity, and dyskinesia with diminished voluntary movements. Asterixis, or flapping tremor of the hands, is elicited by requiring postural tone such as rhythmic squeezing