Covert Hepatic Encephalopathy

Who Should Be Tested and Treated?

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KEYWORDS

• Minimal hepatic encephalopathy • Covert hepatic encephalopathy • Rifaximin
• Probiotics • Encephalapp stroop test • Psychometric hepatic encephalopathy score
• Inhibitory control test • Critical flicker frequency

KEY POINTS

- Covert hepatic encephalopathy (CHE) is a common problem in the cirrhotic population, affecting up to 80%.
- Although it is not diagnosed clinically, it is a serious issue that has shown an increased risk of developing overt hepatic encephalopathy and is independently associated with poor survival and an increased risk of hospitalization.
- The clinical issues complicating CHE include diminished quality of life and work productivity and attention deficits that lead to poor driving performance.
- Rifaximin and probiotics have shown promise for the treatment of CHE.

Covert hepatic encephalopathy (CHE) is an enigmatic complication of portal hypertension. Because it is difficult to diagnose and the manifestations are subtle, CHE has often been ignored. However, emerging data suggest that the ramifications of CHE are substantial and treatment may be beneficial. This article discusses the background and clinical consequences of CHE, diagnostic strategies, and emerging data regarding therapy.

BACKGROUND

Minimal hepatic encephalopathy (MHE), formerly called *subclinical encephalopathy*, and CHE are composed of test-dependent brain dysfunction with clinical consequences in the setting of patients with chronic liver disease who are not disoriented.[1] Minimal encephalopathy indicates that there are no obvious clinical signs of

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encephalopathy. However, as data have accumulated about the impact of minimal encephalopathy on many facets of every day life, it is clear that this term does not accurately describe the entity. The term *CHE*, which includes minimal encephalopathy and grade 1 overt hepatic encephalopathy (OHE), has been adopted (**Table 1**).[1]

CHE is observed within the spectrum of hepatic encephalopathy (HE). It is characterized by abnormalities in central nervous function with impairment in attention, psychomotor speed, visuospatial perception and delayed information processing.[2–5] It differs from OHE in that CHE, by definition, is not confirmed clinically. Specialized testing to identify patients with CHE is required.[1,2] CHE has often been ignored as an important entity because it is difficult to diagnose; there is a notion that if the manifestations are difficult to perceive, it must not be important. However, it is clear that patients with CHE have impaired quality of life (QOL), poor work productivity, and issues with driving.[6–14] Furthermore, the risk of development of OHE is augmented; there is increased associated mortality and a risk of hospitalization.[15–17]

Because CHE is so common in cirrhosis, affecting up to 80% of patients, more interest has arisen in this entity in recent years.[18–21]

DIAGNOSIS

There has been reluctance to perform a diagnostic work-up for CHE for diverse reasons. First, there is a lack of awareness about the problem because it is often not discussed and because the clinical consequences are difficult to observe. Further, the diagnostic tests are somewhat obscure. The lack of standardization of a definitive diagnostic testing regimen has also hindered widespread usage of the tests to diagnose CHE.

Before conferring a diagnosis of CHE, other causes of impaired mentation, such as ischemic neurologic injury, metabolic abnormalities, dementia, or medication-induced cognitive impairment, must be ruled out. Initial evaluation should include eliciting a careful history including prescription medications, over-the-counter products, and usage of alcohol and/or illicit drugs. A neurologic examination should be performed. Finally, the Mini-Mental State Examination (MMSE), a simple test that assesses basic cognitive function and is a screening test for dementia, should be administered.[22] If

Table 1
MHE and CHE

		Description	Manifestation
Minimal	Covert	Psychometric or neuropsychological alterations of tests exploring psychomotor speed/executive functions or neurophysiological alterations without clinical evidence of mental change	There are abnormal results of established psychometric or neuropsychological tests without clinical manifestations.
Grade 1		Trivial lack of awareness Euphoria or anxiety Shortened attention span Impairment of addition or subtraction Altered sleep rhythm	Despite oriented in time and space, patients seem to have some cognitive/behavioral decay with respect to their standard on clinical examination or to the caregivers.

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