Should We Treat Minimal/ Covert Hepatic Encephalopathy, and with What?

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KEYWORDS

- Encephalopathy • Covert hepatic encephalopathy • Overt encephalopathy
- Minimal hepatic encephalopathy

KEY POINTS

- Despite its name, minimal hepatic encephalopathy significantly impacts quality of life and daily function.
- Most patients with cirrhosis develop covert encephalopathy during the natural history of their disease.
- Probiotics, nonabsorbable dissacharides, rifaximin, and L-ornithine-L-aspartate have all been studied for treatment of covert hepatic encephalopathy (CHE).
- Because of lack of readily accessible testing strategies, detection and treatment of CHE remains suboptimal and dependent on regional resources and expertise.

INTRODUCTION

Hepatic encephalopathy (HE) is a heterogeneous class of neuropsychiatric changes seen in cirrhosis in the absence of other organic brain disorders.[1] HE is a spectrum of neurocognitive impairments in cirrhosis that range from abnormal neuropsychiatric testing without clinical evidence of disease (minimal HE [MHE]) to varying degrees of overt clinical findings (overt HE [OHE]).[1] The categories of OHE are broken down by their cause: acute liver failure (type A), bypass (type B), and cirrhosis (type C). The West Haven classification is used to discern the varying degrees of OHE.[2] Much debate has centered on the term "minimal" in MHE because of the concern for trivialization of the neurocognitive impairment in this subgroup by patients and clinicians.[2] The term covert HE (CHE) has been adopted and accepted by the International

The authors have nothing to disclose.

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Clin Liver Dis 19 (2015) 487–495
http://dx.doi.org/10.1016/j.cld.2015.04.002 **liver.theclinics.com**
1089-3261/15/$ – see front matter

Society for Hepatic Encephalopathy and Nitrogen Metabolism to address this misconception.[2] CHE refers to all subclinical HE not detectable by history and physical examination, and includes minimal encephalopathy and West Haven grade I OHE.[1]

CHE is extremely common with up to 80% of patients with cirrhosis being affected.[3] Because of the lack of clinically detectable changes in verbal skills or motor function, the diagnosis of CHE is difficult and requires specialized testing to discern the subtle changes in cognition. The tools currently available for the diagnosis of CHE have been reviewed elsewhere in this issue. Some of these specialized psychometric tests require advanced training to perform and are not readily available in clinical practice. A survey of 137 members of the American Association for the Study of Liver Disease showed only 40% of the respondents routinely tested their patients for CHE. The surveyed group reported that the time and resource allocation required for diagnosis was a major barrier.[4] Because of the lack of an easily performed standardized screening tool and controversy over which patients should be screened CHE remains an underdiagnosed condition.

COVERT ENCEPHALOPATHY: IS IT IMPORTANT?

Deficits in attention and coordination that are seen in CHE affect multiple dimensions of life in a patient with cirrhosis despite not being clinically detectable. Quality of life (QOL) is impacted in patients with CHE and translated into lower QOL scores.[5] Studies by Groeneweg and colleagues[6] have shown significant impact on activities of daily living using the Sickness Impact Profile (SIP). The SIP, which has been validated across a broad range of chronic medical conditions, detects significant impacts on the QOL of patients with cirrhosis with CHE.[1] The SIP uses physical, social, and psychological domains to grade the degree of QOL impairment. The study by Groeneweg and colleagues[6] showed that patients with CHE have significantly reduced scores in all domains. The most affected areas were alertness, home management, work, recreational activities, and sleep.[3]

Falls are a significant burden to health care use and account for 90% of fracture visits in emergency departments.[7] The subclinical visual-motor impairment in patients with CHE puts them at risk for falls.[8] Falls have been shown to be more common in patients with cirrhosis with CHE than without. Patients taking concurrent psychotropic medications were further at risk for falls.[9] The increased prevalence of decreased bone mineral density among patients with cirrhosis places them at increased risk for fracture with falls. In the study by Roman and colleagues[9] one-third of patients with CHE who fell sustained a fracture and hospital stays were longer and more costly in patients with CHE compared with patients with cirrhosis without CHE and healthy control subjects. Of note, all patients who were hospitalized because of falls with CHE experienced hepatic decompensation, whereas no patients hospitalized without CHE experienced decompensation.[9]

The attention and coordination defects seen in CHE also affect the ability to work. Schomerus and Hamster[10] demonstrated that employability is affected by CHE. Blue collar workers whose employment centers on repetitive motion or manual labor are most affected by covert encephalopathy.[1] Direct financial impact comes when these patients are unable to maintain employment or perform at work. Fellow coworkers who may be injured by subclinically impaired patients and caretaker burden contribute to the indirect costs of CHE.

The subclinical impairments in attention and coordination seen in CHE also have significant impact on driving skills. Several studies have highlighted the effect CHE has on driving. Both on-road and simulator testing have consistently shown that