Minimal hepatic encephalopathy: the Role of Brain-Liver Axis

CHING-LIANG LU

Professor National Yang-Ming University/ Attending physician Taipei Veterans General Hospital

Hepatic encephalopathy (HE) is a neuropsychiatric complication of liver cirrhosis which can manifest from subtle cognitive and motor disturbances to stupor and coma. Minimal HE (MHE) is the mildest form of the spectrum. The patients with MHE usually have no recognizable clinical symptoms of HE but have mild cognitive and psychomotor deficits. MHE is associated with impaired health-related quality of life and poor job performance, predicts the development of overt HE, increased hospitalization, and poor survival. Furthermore, the MHE patients in western countries are associated with increased risks of fall accidents and motor vehicle collisions.

MHE is often under diagnosed since such patients have normal verbal function without recognizable clinical symptoms. The MHE patients can only have mild cognitive and psychomotor deficits, which cannot be detected by routine neurological examination. As a consequence, most MHE patients remain undiagnosed and untreated. Tests for MHE can be divided into psychometric and neurophysiological tests. Psychometric tests are further divided into simple paper-and-pencil tests and computerized tests. Psychometric Hepatic Encephalopathy Score (PHES) is an efficient tool for detecting MHE. The PHES combines 5 subtests, i.e., the digit symbol test (DST), number connection test-A (NCT-A), number connection test-B (NCT-B), serial dotting test (SDT), and line tracing test (LTT)—for assessing psychomotor speed and accuracy, visual perception, visuospatial orientation, visual construction, concentration, attention, and working memory. MHE patients can be reliably distinguished from patients with overt HE and from healthy controls by using this simple 'paper and pencil' test. Critical flicker frequency (CFF) test is a neurophysiological test in detecting MHE. The CFF itself is the frequency at which steady fused light begins to flicker. A CFF below 39 Hz is diagnostic for MHE. The CFF test has the advantage of not being confounded by age or education level, which is commonly associated with the PHES test. With these two diagnostic modalities, MHE has been identified in around 30-80% of the cirrhotic patients worldwide.

Recently, an imbalance in stool or colonic mucosal microbiota is linked with systemic inflammation, endotoxemia, and cognitive impairment across the spectrum of HE. Dysbiosis may worsen and contribute to the progression of cirrhosis and HE development. For example, MHE patients have been found to have an overabundance of Streptococcus salivarius, which could increase ammonia production due to its urease activity.

Currently, AASLD does not recommend routine treatment of MHE. Nevertheless, treatment MHE may begin with life style modification, such as avoidance of situations that may lead to

accidents (such as fall) and driving restriction. For pharmacological treatment, evidences show that lactulose can improve psychometric tests and driving simulation. Rifaxamin, a poorly absorbable antibiotics, has also been shown to improve QoL, psychometric tests, and driving simulator performance in MHE patients.