Editorial

Critical flicker frequency: A stethoscope for minimal hepatic encephalopathy evaluation

Praveen Sharma

Department of Gastroenterology, The Ganga Ram Institute for Postgraduate Medical Education and Research, New Delhi, India

Minimal hepatic encephalopathy (MHE) is a very common condition, but is uncommonly evaluated in patients with cirrhosis. It is characterized by cognitive function impairment in the domains of attention, vigilance, and integrative functions without obvious clinical manifestation (1). These psychomotor abnormalities and subtle deficits can only be assessed using specialized psychometric tests, which are not readily available to most practitioners. Not only is availability an issue but also no single method is sufficient for a complete evaluation of all affected domains; hence, we lack a gold standard for MHE identification. MHE is a condition which has more of a theoretical value to most practitioners than a reality in their clinical assessment. This has been assessed in many surveys amongst physicians across various developed and developing countries (2,3).

Minimal hepatic encephalopathy remains an important entity for clinicians to recognize because of its negative impact on a patient's health-related quality of life, association with driving impairment and vehicle accidents, increased rate in the development of overt hepatic encephalopathy (HE), and increased mortality (4-7). Thus, MHE identification and treatment should not be delayed. Symptoms of frequent falls, driving errors, and poor quality of life sometimes are not convincing areas for practitioners to evaluate their patients for MHE. However, convincing them that it affects survival and predicts overt HE similar to how large varices predict future episodes of variceal bleed is a simple way to make them test all their patients for MHE using a simple and readily available tool.

In this issue of the journal, Banu and Mustafa (8) demonstrated the usefulness of critical flicker frequency (CFF) in diagnosing MHE in a small group of patients with cirrhosis (n=70). Taking a cutoff value of <39 Hz, they found that CFF had a sensitivity of 39%, specificity of 82%, and diagnostic accuracy of 70.6% for detecting MHE compared with psychometric hepatic encephalopathy score (PHES) as the gold standard as taken in the majority of studies. In the control group, they did not find any correlation of CFF with age, education, and sex. Similarly, in patients with cirrhosis, CFF shows no correlation with sex and education, whereas weak correlation was seen with age (r=−0.26; p=0.015) and CTP (r=0.26; p=0.016). However, they did not follow up these patients for any future complications of MHE, such as development of overt HE and overall survival, and they did not evaluate for quality of life parameters in these patients to know whether PHES or CFF is better for future complications of MHE. However, this study contributes to the existing scientific knowledge that CFF is an important simple tool, which can supplement physicians in their clinics with tools for the diagnosis of MHE. In my opinion, CFF measurement by HEPAtonorm analyzer for evaluating MHE can be compared with a stethoscope that is used for blood pressure measurement in clinics. If one finds its value to be <39 Hz, the patients can be further evaluated using PHES.

Minimal hepatic encephalopathy is not generally studied because of the absence of any easy method for diagnosis, the lack of effective treatment, and its duration from randomized controlled trials. Any tool which is easy to use and transcends the age and education barrier is a prerequisite for the evaluation of MHE at bedside and improving its management. Validation of its finding across the developing and developed countries would improve its use among practitioners.

Critical flicker frequency measurement by HEPAtonorm for the diagnosis of MHE had a sensitivity of 35%–75% in various studies, depending upon the gold standard and cutoff value of CFF taken (4,9,10). CFF also predicts overt HE and predicts overall survival, irrespective of model for end-stage liver disease (MELD) score. Ampuero et al. (5) found that a decreased CFF predicted

mortality in a well-characterized cohort of 117 patients with cirrhosis, independent of MELD score. MHE identified based on CFF in the setting of a low MELD score did not impact the mortality of the subjects; however, this significantly changed with worsening liver disease. The number of patients with MELD scores of 10–15 and MHE who survived for 5 years (44.4%; 12 of 27) was less than that with MELD scores of >15 without MHE (61.5%; 8 of 13) (p<0.05). Hence, CFF measurement in clinics and value of <39 Hz indicate worse prognosis.

The question now arises whether it can replace PHES or other neurophysiological tests in the near future? CFF is valuable to study alterations in visual signal processing and is suitable for the detection of arousal or attention abnormalities. However, it is not a reliable tool to assess motor function. Hence, CFF could only make a contribution in the detection of some features of MHE, which probably will not be assessed using psychometric tests. Therefore, it may be a better option to use a combination of PHES and CFF till we have a test that is superior over the existing tests. However, PHES as a gold standard for MHE is also not true, as a study by Kircheis et al. (11) showed that PHES, CFF, and a combination of PHES and CFF could not reliably distinguish patients with minimal HE from controls or those with overt HE. So where do we place CFF measurement in the present scenario for the diagnosis and management of MHE? I believe if one measures only CFF in a patient with cirrhosis, one can prognosticate future episodes of overt HE to the patient, if value is <38 Hz, poor survival even if MELD (10-15) is not high and CFF is <39Hz, and diagnosis of MHE with reasonable diagnostic accuracy. It is always better to evaluate than not to with respect to MHE in patients with cirrhosis, as it affects survival and predicts overt HE. Till we have better tools that are not influenced by age, sex, education, availability in clinics, friendliness to people not-well tuned to computer-related applications, CFF is still a very useful tool and is like a stethoscope to the practitioner for evaluating MHE in patients with cirrhosis. I compliment the authors for their study and contribution to scientific knowledge that CFF by HEPAtonorm is a simple tool for the diagnosis of MHE and should be used in day-to-day practice.

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