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Motor vehicle accidents: How should cirrhotic patients be managed?

Kawaguchi T *et al.* Minimal hepatic encephalopathy management

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Abstract

Motor vehicle accidents (MVAs) are serious social issues worldwide and driver illness is an important cause of MVAs. Minimal hepatic encephalopathy (MHE) is a complex cognitive dysfunction with attention deficit, which frequently occurs in cirrhotic patients independent of severity of liver disease. Although MHE is known as a risk factor for MVAs, the impact of diagnosis and treatment of MHE on MVA-related societal costs is largely unknown. Recently, Bajaj *et al* demonstrated valuable findings that the diagnosis of MHE by rapid screening using the inhibitory control test, and subsequent treatment with lactulose could substantially reduce the societal costs by preventing MVAs. Besides the inhibitory control test and lactulose, there are various diagnostic tools and therapeutic strategies for MHE. In this commentary, we discussed a current issue of diagnostic tools for MHE, including neuropsychological tests. We also discussed the advantages of the other therapeutic strategies for MHE, such as intake of a regular breakfast and coffee, and supplementation with zinc and branched chain amino acids, on the MVA-related societal costs.

Key words: Traffic accident; Subclinical hepatic encephalopathy; Coffee; Zinc; Branched chain amino acids

Core tip:

Kawaguchi T, Taniguchi E, Sata M. Motor vehicle accidents: How should cirrhotic patients be managed?

COMMENTARY ON HOT TOPICS

We have read with great interest the recent article by Bajaj *et al*^[1] describing the diagnosis and treatment of minimal hepatic encephalopathy (MHE) to prevent motor vehicle accidents (MVAs), and would strongly recommend it to the readers.

MVAs are serious social issues worldwide^[2]. Various factors are intricately involved in the occurrence of MVAs, and driver illness is an important cause ^[2]. Besides acute myocardial infarction, epileptic seizure, and hypoglycemia related to the use of anti-diabetic agents, liver cirrhosis with MHE has been reported to increase the risk of MVAs^[3-6]. Although MHE occurs in up to 80% of patients with chronic liver disease ^[3] and diagnostic tools and therapeutic strategies for MHE exist^[7-11], little information is available about the management of patients with liver cirrhosis with regard to preventing MVAs and subsequently reducing the associated societal costs.

In their study, Bajaj *et al*^[1] performed a cost-effectiveness analysis to identify management strategies for the diagnosis and treatment of MHE in patients with liver cirrhosis to reduce MVA-related societal costs. They found that the diagnosis of MHE by rapid screening using the inhibitory control test (ICT), and subsequent treatment with lactulose could substantially reduce societal costs by preventing MVAs^[1]. This is a significant study, and we agree with the authors about the benefits of the use of the diagnostic test and therapeutic management. However, we suggest that the management strategy should be modified to some extent for use in general medical institutions to prevent MVAs on a larger scale.

The ICT is a computerized test of attention and response inhibition that has been used to characterize attention deficit disorders^[12]. The ICT consists of the presentation of several letters at 0.5 s intervals, while the subject is instructed to respond or inhibit their

response to the specific letter^[13]. The ICT is considered reliable and sensitive for the diagnosis of MHE^[5, 13]. In addition, unlike standard neuropsychological tests, ICT results are significantly associated with the future occurrence of MVAs ^[3]. However, the test takes approximately 30 min to complete and patients need to be familiar with computer operation. Furthermore, validation and standardization are required for each population, and therefore, so far, the ICT is not universally accessible. Similarly, other diagnostic tools for MHE also require trained personnel and specialized equipment ^[11]. In fact, an American Association for the Study of Liver Disease (AASLD) survey showed that the majority of AASLD members are not able to test for MHE because of a lack of time, resources, and suitable personnel^[14]. Along with Bajaj *et al*, we propose that rapid and simple tools for the diagnosis MHE should be developed urgently, such as biochemical tests or virtual reality driving simulations.

Lactulose has been used to treat hepatic encephalopathy since 1966 ^[15]. Lactulose reduces blood ammonia levels and improves overt hepatic encephalopathy as well as MHE^[7]. In their study, Bajaj *et al*^[1] have demonstrated the benefits of lactulose therapy on the occurrence of MVAs and MVA-related societal costs. However, compliance with lactulose treatment is generally poor, primarily because of its side-effects such as abdominal discomfort^[16, 17]. Recently, other therapeutic strategies for MHE have been reported. First, as prolonged periods of fasting are linked to the development of MHE, having a regular breakfast improves the attention and executive functions of cirrhotic patients with MHE^[18]. Second, coffee intake improves cognitive function in elderly people as well as in patients with type 2 diabetes mellitus^[19, 20]. Although the beneficial effects of coffee on cognitive function have never been investigated in cirrhotic patients, insulin resistance is frequently seen in patients with chronic liver disease^[21-23]. In

addition, coffee consumption is known to improve hepatic inflammation and fibrosis in patients with chronic liver disease^[24]. Third, the blood ammonia level is regulated by the activity of ornithine transcarbamoylase and zinc is a coenzyme required for its up-regulation^[25]. Oral zinc supplementation improves hyperammonemia as well as hepatic encephalopathy, as seen in a double-blind randomized controlled trial^[26]. Finally, a decrease in serum branched chain amino acids (BCAA) levels is a feature of chronic liver disease^[27]. BCAA is a source of glutamate, which detoxifies ammonia by glutamine synthesis in the skeletal muscle and brain^[28]. Therefore, BCAA enhances the detoxification of blood ammonia by incorporating ammonia in the process of glutamine production and is currently used for treating patients with hepatic encephalopathy^[29]. Thus, a therapeutic approach comprising the intake of a regular breakfast and coffee, and supplementation with zinc and BCAA may improve the cost-effectiveness of MVA-related events in cirrhotic patients with MHE (Figure 1).

Prevention of MVA by the diagnosis and treatment of MHE is an important component in the management of patients with liver cirrhosis. Collaborative researches among medical institutions, automobile companies, and governmental sectors may help further prevent MVAs and subsequently reduce MVA-related societal costs.

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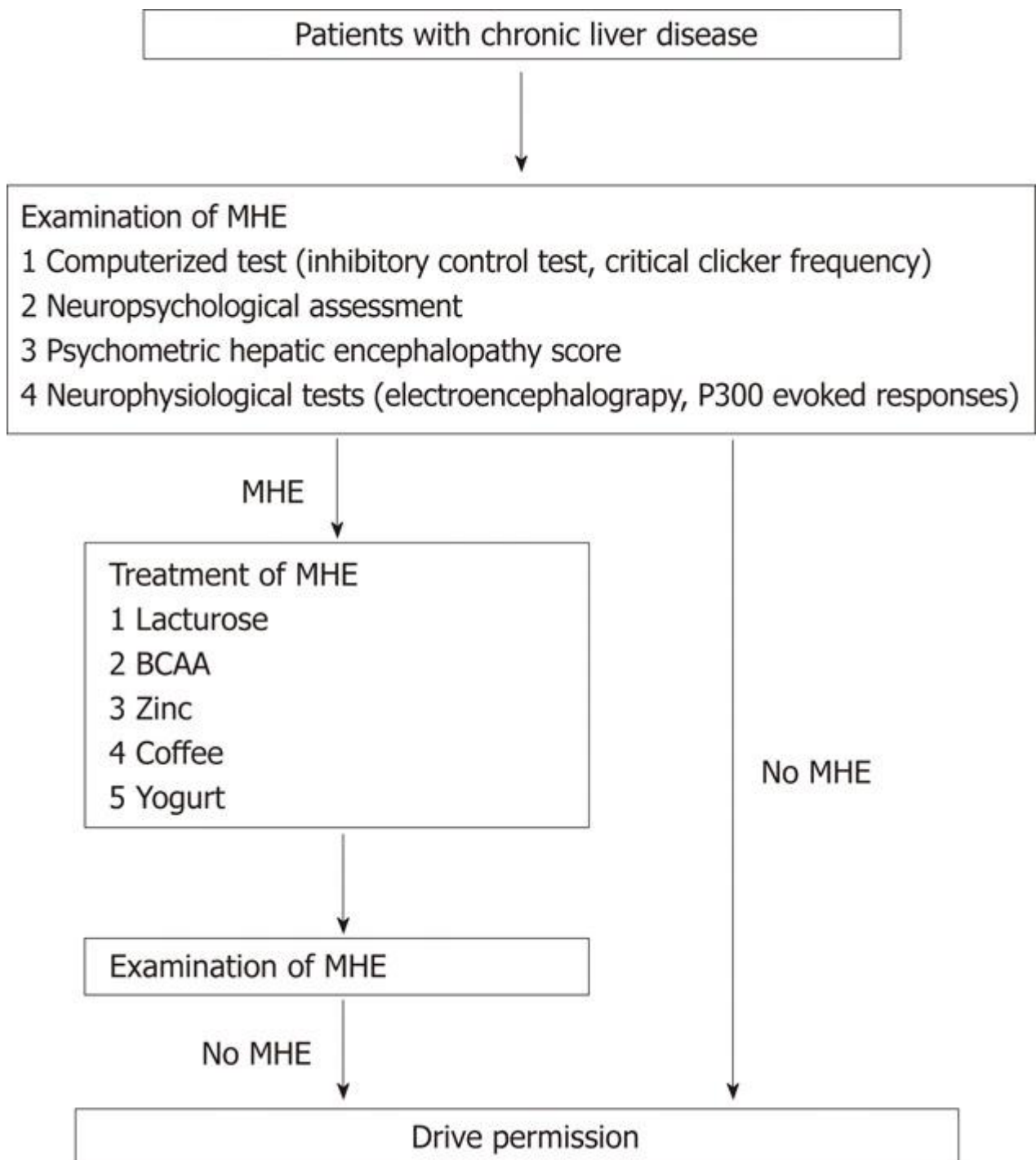


Figure 1 A proposed flow chart of drive permission for patients with chronic liver disease. MHE: Minimal hepatic encephalopathy; BCAA: Branched chain amino acids.