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OVERVIEW ON MANAGEMENT OF HEPATIC ENCEPHALOPATHY

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ABSTRACT
Minimal hepatic encephalopathy (MHE) is a neurocognitive dysfunction that is present in the majority of patients with cirrhosis. MHE has a characteristic cognitive profile that cannot be diagnosed clinically. This cognitive dysfunction is independent of sleep dysfunction or problems with overall intelligence. MHE has a significant impact on quality of life, the ability to function in daily life and progression to overt hepatic encephalopathy. Driving ability can be impaired in MHE and this may be a significant factor behind motor vehicle accidents. A crucial aspect of the clinical care of MHE patients is their driving history, which is often ignored during routine care and can add a vital dimension to the overall disease assessment. Driving history should be an integral part of the care of patients with MHE. The preserved communication skills and lack of specific signs and insight make MHE difficult to diagnose. The predominant strategies for MHE diagnosis are psychometric or neurophysiological testing. These are usually limited by financial, normative or time constraints. Studies into inhibitory control, cognitive drug research and critical flicker frequency tests are encouraging. These tests do not require a psychologist for administration and interpretation. Lactulose and probiotics have been studied for their potential use as therapies for MHE, but these are not standard-of-care practices at this time. Therapy can improve the quality of life in MHE patients but the natural history, specific diagnostic strategies and treatment options are still being investigated.

KEYWORDS: Minimal hepatic encephalopathy (MHE).

➢***Treatment of minimal and covert HE***

Several studies used a variety of agents including probiotics, lactulose and rifaximin in minimal HE, most studies have been for less than 6 months and do not reflect the overall course of the condition.[1] Trials expand from small open-label trials to larger, randomized–controlled studies using various treatments.[2] Most studies have shown an improvement in the underlying cognitive status but the mode of diagnosis has varied considerably among studies.[3]

Little of studies used clinically relevant endpoint, it was shown in an open-label study that lactulose can prevent development of the first episode of overt HE but the study needs to be replicated in a larger study in a blinded fashion before firm recommendations can be made.[4] Studies using lactulose and rifaximin have shown improvement in quality of life and also in driving simulator performance.[5] Probiotics have also been used but the open-label nature, varying amounts and types of organisms and different outcomes make them difficult to recommend as therapeutic options at this time.[6] Owing to the multiple methods used to define minimal and covert HE, varying endpoints, short-term treatment trials and differing agents used in trials to date, routine treatment for minimal HE is not recommended at this stage.[7] Exceptions could be made on a case-by-case basis using treatments that are approved for overt HE, particularly for patients with covert HE and West-Haven grade I HE.[8]

➢***Nutrition***

Modulation of nitrogen metabolism is crucial to the management of all grades of HE and nutritional options are relevant.[9] Malnutrition is often under-diagnosed, and about 75% of patients with HE suffer from moderate to severe protein-calorie malnutrition with loss of muscle mass and energy depots. Chronic protein restriction is detrimental, as the patients' protein requirements are relatively greater than normal patients and they are at risk of accelerated fasting metabolism. Sarcopenia has been proven to be an important negative prognostic indicator in cirrhotic patients.[10]

The therapy is refeeding by moderate hyperalimentation. Small meals evenly distributed throughout the day and a late-night snack should be encouraged, with avoidance of fasting.[11] The hyperalimentation should be given orally to patients who can cooperate, by gastric tube to patients who cannot take the required amount and parenterally to

other patients.[12] There is consensus that low protein nutrition should be avoided for patients with HE. Oral BCAA-enriched nutritional formulation may be used to treat HE and generally improves the nutritional status of cirrhotic patients, but intravenous BCAA for an episode of HE has no effect.[13]

Non-absorbable disaccharides

Lactulose is usually used as initial treatment for overt HE, a large meta-analysis of trial data did not completely support the efficacy of lactulose for the treatment of overt HE and cost considerations alone added to the argument in support of lactulose.[14] Lactitol is similar to lactulose and, based on small meta-analyses of even smaller trials, it appears to be more effective.[15] In populations with a high prevalence of lactose intolerance, the use of lactitol has been suggested.[16] Stool-acidifying enemas (lactose and lactulose) were superior to tap-water enemas in a very small study.[17]

Lactulose dosing should be initiated with 25 milliliters of lactulose syrup every 1–2 hours until at least two soft or loose bowel movements per day are produced. Afterwards, the dosing is titrated to maintain two to three bowel movements per day.[15]

Probiotics: Probiotics represent an attractive therapeutic agents in the strategies of treatment of HE. Considered, natural therapy, as occasionally considered as complementary medicine, it is relatively well tolerated even in cirrhotic patients.[19] The three suggested mechanisms through which probiotics exerts their efficacious effects and disrupt the pathogenesis of HE include the following.[20]

(1) Decreasing total ammonia in the portal blood by:
(a) decreasing bacterial urease activity;
(b) decreasing ammonia absorption by decreasing pH;
(c) decreasing intestinal permeability;
(d) improving nutritional status of gut epithelium.
(2) Decreasing inflammation and oxidative stress in the hepatocytes leading to increased hepatic clearance of ammonia and toxins.
(3) Decreasing uptake of other toxins.

Probiotics have had encouraging results in improving psychometric test results and severity of liver disease (with improvement in the Child-Turcotte-Pugh score) in some studies.[21,22] screened 97 consecutive outpatients with cirrhosis but without overt HE and reported that the administration of synbiotics (probiotics and fermentable fibre) increased the fecal content of non-urease producing Lactobacillus species at the expense of other potentially pathogenic species such as Escherichia coli and Staphylococcus species. Such modulation of gut flora was associated with lowering of blood ammonia levels and reversal of MHE in 50% of patients.[22]

However, a recent meta-analysis revealed the lack of well-designed trials.[23] Larger followup studies are required to further validate the therapeutic potential of probiotics and to determine the sustained efficacy and tolerability before they can be recommended as standard treatment.

CONCLUSION

Therapeutic challenges for OHE depend on the acuity and severity of the clinical condition. At this time, therapy for MHE needs to await long-term trials that focus on clinically relevant outcomes. The overall management consists of properly identifying OHE, gauging its severity, treating potential precipitating factors and using treatments specifically directed towards OHE. Out-patient management goals for OHE are prevention of recurrence and improvement in daily functioning. At this time, lactulose and rifaximin have emerged as leading therapeutic options for in-patient and out-patient OHE therapy in the US. Liver transplant work-up in these individuals needs to be initiated to ensure a lasting improvement in mental status.

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