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Original Article

Comparison of the Efficacy of *Lactobacillus rhamnosus* GG and Lactulose Treatments in Minimal Hepatic Encephalopathy

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ABSTRACT

Objective: Minimal hepatic encephalopathy is a condition characterized by decreased perception and consequently deterioration in quality of life, and there is still limited data on its treatment. The aim of this study is to compare the efficacy of lactulose and *Lactobacillus rhamnosus* GG treatments by critical flicker frequency test in minimal hepatic encephalopathy patients.

Methods: Patients with a critical flicker frequency test result of <39 Hz were considered to have minimal hepatic encephalopathy. Eighty-four minimal hepatic encephalopathy patients were divided into 3 groups as lactulose, *Lactobacillus rhamnosus* GG, and control group. Critical flicker frequency control was performed 4 weeks after treatment. Critical flicker frequency values before and after treatment were compared according to the treatment groups and evaluated.

Results: Minimal hepatic encephalopathy was detected in 84 (54.5%) of 154 cirrhosis patients. Of the patients with minimal hepatic encephalopathy, 31 (36.9%) received lactulose, 31 (36.9%) *Lactobacillus rhamnosus* GG treatment, and 22 (26.2%) did not receive any treatment. In patients with minimal hepatic encephalopathy compared to those without minimal hepatic encephalopathy, there were statistically significant differences in terms of age ($P = .003$), body mass index (BMI) ($P = .019$), albumin ($P < .001$), sodium ($P = .010$), model for end-stage liver diseases score ($P < .001$), and Child Pugh Classification (CHILD) score ($P < .001$).There was no significant difference between cirrhosis etiology and treatment response ($P = .535$). Statistically significant increase was found in critical flicker frequency values in the lactulose ($P = .011$) and *Lactobacillus rhamnosus* GG ($P = .007$) groups after treatment. No statistically significant difference was found in the placebo group ($P = .804$). There was no statistically significant difference between lactulose and *Lactobacillus rhamnosus* GG ($P = .576$).

Conclusion: In the treatment of minimal hepatic encephalopathy, *Lactobacillus rhamnosus* GG treatment is as effective like lactulose treatment and can be used safely.

Keywords: Critical flicker frequency, lactobacillus rhamnosus, lactulose, minimal hepatic encephalopathy

INTRODUCTION

Hepatic encephalopathy (HE) is a brain dysfunction that can be associated with hepatic failure, cirrhosis, or portosystemic shunts, can range from subclinical disease to coma, and is accompanied by neurological or psychiatric abnormalities.[1] In minimal hepatic encephalopathy (MHE), no mental or neurological disorder is detected during clinical examination. Minimal hepatic encephalopathy is the early stage of covert hepatic encephalopathy (CHE), which can be diagnosed by neurophysiological and psychometric tests.[2] There is no obvious impairment of cognitive functions in MHE. However, there is a significant decrease in the quality of life in these patients due to decreased visual perception, impaired ability to drive, and difficulty in performing tests that require psychomotor speed and attention.[3]

Minimal hepatic encephalopathy is diagnosed by neurophysiological and psychometric tests. Psychometric tests can be affected by factors like age and education level and standardization. In addition, these tests take a long time to perform and, if repeated, may give erroneous results because patients learn the tests and memorize them. Test results may be influenced by these disadvantageous situations.[4] Other tests used in the diagnosis of MHE are Inhibitory Control Test, Cognitive Drug Research Test, Scan Test, STROOP App Test, and the critical flicker frequency (CFF) test.[5] The level of education, age of the patient, the fact that the test is not affected by frequent repetitions, and its prediction of overt hepatic encephalopathy (OHE) make the CFF test superior to the others. In addition, improvement with treatment observed in the test results is one of the advantages of the CFF test.[6] Once CHE develops in patients with cirrhosis,

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50% of the patients develop OHE, an indication that the prognosis will be poorer within three years. After the development of OHE, neuropsychiatric disorders may become persistent and unresponsive to medical therapy. In addition, it can cause major problems which can require liver transplantation. As a result, treatment of CHE is important.[7]

There is still no consensus on which treatment scheme is the best once CHE is detected. Probiotics, non-absorbable disaccharides, rifaximin, and L-ornithine L-aspartate (LOLA) are currently the most studied and recommended therapeutic agents in the treatment of CHE.[8] The common goal of treatments is to reduce the formation and absorption of ammonia and other toxins in the intestine. Lactulose has properties such as acidifying the feces, increasing beneficial organisms in the intestine, and shortening the colonic transit time, in addition to its laxative effect.[9] The effect of dysbiosis on the development of HE is currently well known, and there are many studies showing that the use of probiotics reduces episodes of HE.[10] Rifaximin is a gastrointe stinal-specific antibiotic, and when used together with lactulose has been shown to improve cognitive functions and to decrease ammonia levels.[11]

Although there are studies on the use of lactulose and probiotics in the treatment of MHE, the number of studies evaluating the comparison of these treatments is limited. Many different probiotics have been used in the treatment of MHE, and there are no studies on *Lactobacillus rhamnosus* GG (LbGG). The first aim of our study was to determine the prevalence of MHE in patients with cirrhosis. It was also aimed to compare the efficacy of lactulose or probiotic (LbGG) treatments on MHE in patients followed up for cirrhosis and diagnosed with MHE by the CFF test.

METHODS

Seven hundred eighty-four patients diagnosed with liver cirrhosis and admitted to the hepatology outpatient clinic of Gaziantep University Medical Faculty Hospital were evaluated retrospectively. The patients were diagnosed with cirrhosis by evaluating together with anamnesis, physical examination, laboratory findings, imaging methods, and/or liver biopsy. Since 51 patients died due to various reasons, the files of the remaining 723 patients were evaluated in detail. The exclusion criteria were history of OHE, alcohol use in the last 3 months, receiving treatment for HE, visual and/or hearing impairment, hepatocellular cancer (HCC) or other malignancy, active gastrointestinal bleeding, electrolyte imbalance, alcohol-induced liver cirrhosis, presence of a psychiatric or neurological disease, use of an anti-psychotic or sedative, etc., presence of overt porto-systemic shunt, previous shunt surgery, use of antibiotics, lactulose or LOLA in the last 6 weeks, presence of active infection, and not giving written consent for inclusion in the study. A total of 154 patients who met the inclusion criteria, aged above 18 years, and did not have findings suggestive of OHE (euphoria, depression, sleep disorders, impaired handwriting, changes in mental functions, memory disorders, mild disorientation, and coordination disorders) were included in the study.

Main Points

- It may be recommended that patients with advanced Child-Pugh stage and high model for end-stage liver diseases scores should be approached more carefully in terms of minimal hepatic encephalopathy (MHE) screening.
- The etiology of cirrhosis did not play an important role in the development of MHE.
- In our study, the treatment efficacy for MHE was found to be higher in the groups given lactulose and *Lactobacillus rhamnosus* GG compared to the placebo group. However, no superiority was found between the 2 treatment groups.

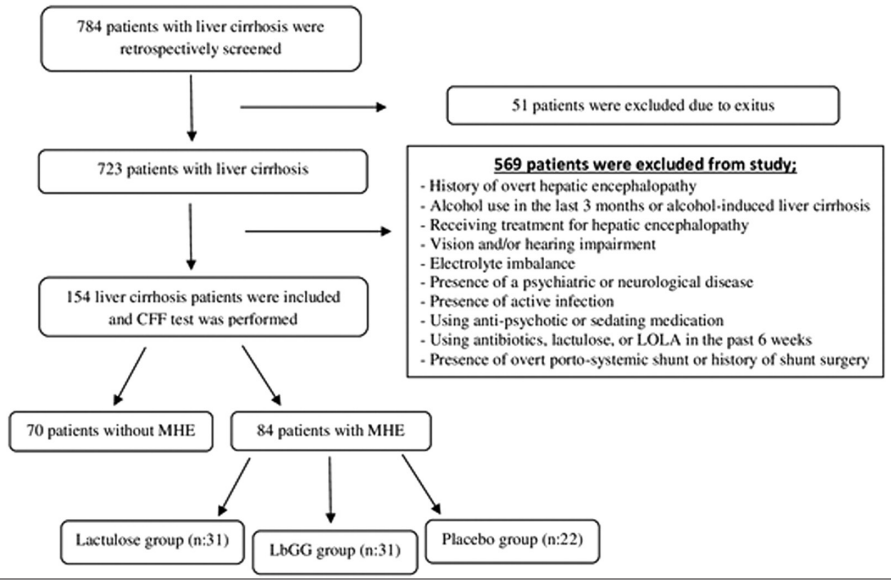
Medical history of patients was obtained, and complete blood count and biochemical tests were requested for all patients. The etiology of cirrhosis (viral, cryptogenic, autoimmune, metabolic, etc.) and complications of cirrhosis were recorded from patient files. Child-Pugh and model for end-stage liver diseases (MELD) scores were calculated. Based on the presence of MHE, patients were compared according to their demographic characteristics, laboratory parameters, BMI, Child-Pugh, and MELD scores. The patients were classified as compensated and decompensated cirrhosis according to the history of ascites, jaundice, and varicose bleeding other than HE. The BMI of the patients was calculated as kg/m^2. The literacy status of the patients was recorded.

All patients underwent the CFF test. Eighty-four patients with MHE based on the CFF test were divided into 3 groups. The first group (n = 31) was given lactulose (duphalac 3.335 mg/5 mL) oral solution 1-2 times a day to provide soft stools. The second group (n = 31) was given probiotic tablets containing 6 billion LbGG (kaleidone 60 mg capsule) twice a day. No treatment was given to the third group (n = 22) (Figure 1). The patients underwent the CFF test at the time of their first tests and 30 days after treatment. Patients with follow-up CFF values of >39 Hz after the MHE treatment were considered to have benefited from the treatment. The relationship between treatment benefit and the treatment groups, laboratory parameters, demographic characteristics, cirrhosis etiology, and cirrhosis complications were then compared. Ethics committee approval was obtained from the Ethics Committee of Gaziantep University (Date: July 24, 2017, Decision no: 2017/280). Oral and written explanations were given to the patients included in the study and their consent was obtained.

Minimal Hepatic Encephalopathy Evaluation

The presence of MHE was evaluated with the CFF test. This is a test that measures the highest range of flickering of light from a light source perceivable by the patient. The test was performed using a HEPAtonorm analyzer (R&R Medi-Business Freiburg GmbH, Freiburg, Germany). Each patient was taken to a comfortable, quiet test room away from external stimuli. Each patient was told how to perform the test. To perform this test, a device was attached to the patient's head, and after a steady red light arrived in the patient's eyes, the patient was asked to observe and follow this red light and press the button in his/her hand when he/she noticed that the light was flickering. After this test was repeated several times by the patient, recording was started.

Figure 1. Flow chart of the study. LOLA, L-ornithine L-aspartate; MHE, minimal hepatic encephalopathy; CFF, critical flicker frequency; LbGG, *Lactobacillus rhamnosus* GG.



The test was performed on the patients 9 times and recorded. The mean and standard deviation of these 9 tests were then determined. Patients with a CFF test result of <39 Hz were considered to have MHE.

Diet and Drug Habits

Patients with ascites were recommended to take a salt-poor diet (<2 g sodium) throughout the study. Protein intake was not restricted and all patients were encouraged to take a diet containing 1-1.5 g/kg/day of protein. Decision to give treatment to patients whose CFF results were not normal was made from the files. Treatments received by the patients were recorded. It was confirmed that none of the patients was treated with rifaximin, LOLA, lactulose, or LbGG. The treatment of patients who were taking diuretics, spironolactone for ascites, or beta-blocker therapy for varicose bleeding prophylaxis was not discontinued.

Statistical Analysis

Data evaluations were made using software package programs Statistical Package for the Social Sciences 22 (SPSS Inc., Chicago, IL, ABD). Data were expressed as mean ± SD. The Student's *t* test, chi square, dependent groups *t*-test, Mann-Whitney *U* test, and Kruskal–Wallis analysis were used together with descriptive statistics. The statistical significance value was considered as $P < .05$.

RESULTS

The medical records of 784 patients with cirrhosis were evaluated. Seventy-nine (51.3%) of the 154 patients with cirrhosis included in the study based on the exclusion criteria were male. The mean age was 55.1 ± 13.4 years. No statistically significant difference was found between the mean ages by gender ($P = .087$). The mean BMI of the patients was 27.8 ± 4.4 kg/m^2, while the mean BMI of female patients was found to be statistically significantly higher than of the men (29.1 ± 4.8 kg/m^2 vs. 26.5 ± 3.6 kg/m^2, respectively, $P < .001$). The mean value for the CFF test applied to the patients was 40.0 ± 5.9 (min = 26.9, max = 56.3). Patients with a CFF test result of <39 Hz were considered to have MHE. Minimal hepatic encephalopathy was detected in 84 (54.5%) of the patients.

Comparison of the demographic characteristics, laboratory parameters, MELD, and CHILD scores of the patients according to the presence of MHE demonstrated that there was a significant difference between the 2 groups in terms of age ($P = .003$), BMI ($P = .019$), albumin ($P < .001$), sodium ($P = .010$), MELD scoe ($P < .001$), and CFF values ($P < .001$) (Table 1). Of the patients without MHE, 48 (68.5%) were Child A, 21 (30%) were Child B, and 1 (1.5%) was Child C. Of the patients with MHE, 24 (28.5%) were Child A, 52 (61.9%) were Child B, and 8 (9.6%) were Child C. The rate of developing MHE was observed to be statistically significantly higher with increased Child-Pugh scores ($P < .001$) (Table 1).

With respect to the etiology of cirrhosis, 13 (15.4%) of the patients with MHE were reported to be cryptogenic, 13 (15.4%) had nonalcoholic steatohepatitis, 25 (29.7%) had Hepatitis C virus (HCV), 19 (22.6%) had Hepatitis B virus (HBV), 3 (3.6%) had Budd-Chiari syndrome, 2 (2.4%) had Wilson's disease, 3 (3.6%) had celiac disease, 3 (3.6%) had portal vein thrombosis, 2 (2.4%) had primary biliary cirrhosis while 1 (1.2%) had autoimmune hepatitis. There was no statistically significant relationship in terms of development of MHE in the patients according to the etiology of cirrhosis ($P = .573$) (Table 2). Of the patients without MHE, 58 (82.8%) had compensated cirrhosis, while 12 (12.8%) had decompensated cirrhosis. Of the patients without MHE, 41 (48.8%) had compensated cirrhosis, while 43 (51.2%) had decompensated cirrhosis. When compared according to the type of cirrhosis, the rate of MHE was found to be statistically significantly higher in patients

Table 1. Comparison of Demographic Characteristics and Laboratory Parameters of Patients According to the Presence of Minimal Hepatic Encephalopathy

Parameters	Non-MHE	MHE	*P*
Age	51.5 ± 13.7	58.0 ± 12.5	.003
BMI (kg/m²)	28.5 ± 4.6	26.9 ± 3.9	.019
WBC (µL)	4502 ± 1714	4763 ± 2194	.419
Hb (g/dL)	12.6 ± 2.1	12.2 ± 2.2	.189
PLT (µL)	96 940 ± 62 435	99 310 ± 51 930	.798
AST (U/L)	46.3 ± 27.2	43.8 ± 23.4	.532
ALT (U/L)	33.5 ± 26.8	29.3 ± 17.6	.247
INR	1.5 ± 0.2	1.6 ± 0.3	.132
Kreatinin (mg/dL)	0.7 ± 0.3	0.8 ± 0.2	.100
Albumin (g/dL)	3.8 ± 0.4	3.0 ± 0.4	.001
Total bilirubin (mg/dL)	1.7 ± 1.7	1.8 ± 1.5	.692
Sodium (mmol/L)	138.3 ± 2.6	133.4 ± 3.5	.010
MELD	13.9 ± 3.1	16.6 ± 3.8	.001
CFF	45,3 ± 4,1	35.7 ± 2.9	.001
Child A	48 (66.7%)	24 (33.3%)	.001
Child B	21 (28.8%)	52 (71.2%)	.001
Child C	1 (11.1%)	8 (89.9%)	.001

MHE, minimal hepatic encephalopathy; CFF, critical flicker frequency; INR, International normalized ratio; ALT, alanine aminotransferase; AST, aspartat aminotransferase; HBG, hemoglobine; PLT, platelet.

with decompensated cirrhosis than in patients with compensated cirrhosis (78.2% vs. 41.4%, respectively, $P < .001$).

Patients with MHE were divided into 3 groups as lactulose (n = 31, 36.9%), LbGG (n = 31, 36.9%) and placebo (n = 22, 26.2%) patient groups. There was no significant difference between the treatments received and the treatment response according to the etiology of cirrhosis ($P = .535$). When the CFF values before and after the treatment were compared according to the groups, there was a statistically significant increase in the CFF values in the lactulose ($P = .011$) and LbGG ($P = .007$) groups after the treatment. No statistically significant difference was found in the placebo group ($P = .804$) (Table 3). Minimal hepatic encephalopathy was found to be resolved (CFF > 39 Hz) in 24 (77.4%) of the 31 patients with MHE who were treated with lactulose and in 22 (70.9%) of the 31 patients who were treated with LbGG. However, no statistically significant difference was found between the 2 groups ($P = .576$).

Table 2. The Relationship Between the Development of Minimal Hepatic Encephalopathy According to the Etiology of Cirrhosis

	Non-MHE		MHE		
Etiology of Cirrhosis	(n)	(%)	(n)	(%)	*P*
Cryptogenic	11	45.8	13	54.2	.573
NASH	13	50	13	50	
Hepatitis C	14	35.9	25	64.1	
Hepatitis B	18	48.6	19	51.4	
Budd-Chiari syndrome	4	57.1	3	42.9	
Wilson disease	5	71.4	2	28.6	
Celiac disease	2	40.0	3	60.0	
Portal vein thrombosis	1	25.0	3	75.0	
Primary biliary cirrhosis	1	33.3	2	66.7	
Autoimmune hepatitis	1	50.0	1	50.0	

MHE, minimal hepatic encephalopathy; NASH, nonalcoholic steatohepatitis.

There was no statistically significant difference between the improvement of MHE after treatment and age, BMI, laboratory parameters, and MELD scores of the patients ($P > .05$) (Table 4). No statistically significant difference was also found when the relationship between treatment benefit status and the Child-Pugh classification and cirrhosis status (compensated-decompensated) was examined ($P = .138$, $P = .175$, respectively).

DISCUSSION

Contrary to OHE, MHE is a condition which is rarely recognized because there are no clinically detectable symptoms of mental and neurological dysfunction.[12] Minimal hepatic encephalopathy can significantly affect the daily life of patients by impairing many factors such as learning and driving skills, job performance, and cognitive function. Detection and treatment of MHE as early as possible is very important for improving the outcomes of patients with cirrhotic.[13,14]

Cognitive deficits in patients with MHE are hard to detect during routine physical or neurological assessment. Neuropsychological and/or neurophysiological tests should be performed to detect such deficits. Neurophysiological tests are electroencephalogram, evoked potentials, and CFF. Neuropsychological tests include number combination test, finger connection test, and line and circle drawing tests. Imaging methods used to diagnose MHE are computed tomography, magnetic resonance imaging, and magnetic resonance spectroscopy.[15]

For the diagnosis of MHE, a test which can allow detection of neuropsychiatric disorders shows similar results when repeated and does not give different results according to the person performing the test should be used.[16] The first study conducted by Kircheis et al[17] suggested that retinal gliopathy occurring in cirrhosis may reflect subclinical hepatic encephalopathy and cerebral gliopathy. Another study suggested that one of the most sensitive methods in the diagnosis of MHE was the CFF test, and when the threshold value was taken as <39 Hz, the sensitivity was 96% and the specificity was 77%.[18] In the study conducted by Romero-Gómez et al., when the significant threshold value for the diagnosis of MHE was taken as <38 Hz, the sensitivity was found as 72.4% and the specificity as 77.2%, and this was considered the best value.[19] We used the CFF test because education level, patient age, and frequent repetitions do not affect the test; it is a non-invasive, easily applicable method, and improvement can be shown with follow-up tests after treatment.

Table 3. Comparison of CFF Values Before and After Treatment According to Treatment Groups

	CFF Values Before Treatment			CFF Values After Treatment			
Treatment Groups	**Avarage ± SD**	**Min**	**Max**	**Avarage ± SD**	**Min**	**Max**	***P***
Lactulose	34.9 ± 3.1	26.9	37.8	40.9 ± 3.9	30.9	45.1	.011
Probiotic (LbGG)	35.3 ± 3.1	27.6	37.3	41.7 ± 5.4	28.3	52.8	.007
Placebo	37.2 ± 1.5	33.5	37.8	37.1 ± 3.3	30.6	43.5	.804

CFF, critical flicker frequency; LbGG, *Lactobacillus rhamnosus* GG.

The prevalence of MHE may vary between 23% and 56% in different studies. In the study conducted by Kircheis et al.[17] the rate of MHE was found to be 27%. In this study, it was suggested that, the fact that 65% of the patients in the study were in the Child A group may have caused this difference. In 2 different studies, the prevalence of MHE was found to be 53% and 60%, while the mean ages of the patients were 41 and 39.[18,20] In another study, it was shown that there is a correlation between CFF test values and age in both the healthy group and the cirrhosis patient group. Dhiman et al[21,22] showed that CFF values decreased with age and that age-adjusted values of the CFF test may be necessary. The prevalence of MHE was 54.5% in our study, although these studies show parallelism with our study. The mean age was 55.1, and a significant correlation was found between age and MHE. However, no correlation was found between gender and education level.

One of the factors affecting MHE is the stage of cirrhosis. In the study conducted by Romero-Gómez et al.[19] a weak correlation was found between CFF test results and Child-Pugh staging; however, no correlation was found with the MELD score.[19] Two different studies supported the relationship between MHE and Child-Pugh.[23] In our study, a statistically significant relationship was found between MELD score, Child-Pugh stage, and MHE, supporting the studies mentioned. In line with this information, it can be suggested that the more advanced and complicated the cirrhosis was, the higher the MHE detection rate. However, indicators that predict the progression of cirrhosis may be markers for the development of MHE. In this patient group, screening for MHE should be performed even if there is no OHE.

Factors contributing to the development of MHE are similar to those for OHE, and these are hyperammonemia, sarcopenia, excessive bacterial growth, dysbiosis, and increase in inflammatory cytokines and hyponatremia.[20] Recently, it has been reported that intestinal microbiota is impaired in patients with cirrhosis and this dysbiosis plays a substantial role in the formation of ammonia.[21] Probiotics reduce inflammation and oxidative stress in hepatocytes. In addition, it also reduces intestinal permeability and absorption of ammonia by regulating impaired microbiota in the intestines by colonic acidification. It also plays an important role in the regulation of immune response.[22]

There are many studies evaluating the efficacy of probiotic treatment in cirrhotic patients with MHE. In a meta-analysis including 14 different randomized controlled trials in which a total of 1132 patients were evaluated, many

Table 4. Comparison of Age, BMI, Laboratory Values, and MELD Score According to Benefit from Treatment

	Benefit from Treatment			No Benefit from Treatment			
	Avarage ± SD	**Min**	**Max**	**Avarage ± SD**	**Min**	**Max**	***P***
Age	54.1 ± 14.6	20	72	60.3 ± 11.6	24	83	.126
BMI	27.2 ± 4.5	20.8	35.1	29.4 ± 4.9	20.2	41.6	.121
WBC	4592 ± 2114	2430	10 390	4920 ± 2456	1560	14 550	.495
HGB	11.8 ± 1.7	8.8	14.4	12.1 ± 2.3	8.8	18.0	.895
PLT	89 611 ± 40 733	52 000	2 27 000	1 05 886 ± 58 508	32 000	38 5000	.147
AST	45.3 ± 24.4	22	125	40.5 ± 18.5	14	107	.514
ALT	27.9 ± 15.5	10	76	26.0 ± 13.1	5	76	.792
INR	1.6 ± 0.6	1.2	3.9	1.6 ± 0.3	1.2	2.7	.407
Kreatinin	0.7 ± 0.2	0.4	1.2	0.9 ± 0.3	0.5	1.8	.149
Albumin	3.0 ± 0.3	2.6	3.6	3.0 ± 0.4	1.2	3.8	.851
Bilirubin	1.7 ± 1.0	0.6	4.7	1.7 ± 1.1	0.3	5.7	.901
Sodium	134.2 ± 4.4	125	142	134.2 ± 3.6	125	144	.895
MELD	16.2 ± 4.0	11	26	17.1 ± 4.2	10	28	.427

MELD, model for end–stage liver diseases; BMI, body mass index; WBC, white blood cell; ALT, alanine aminotransferase; AST, aspartat aminotransferase; HBG, hemoglobine; PLT, platelet.

different probiotics (*Pediococcus pentosaceus*, *Leuconostoc mesenteroides*, *Lactobacillus plantarum*, *Lactobacillus acidophilus*, *Bifidobacterium bifidum*, *Streptococcus thermophilus*, *Bifidobacterium longum*, *Bifidobacterium infantis*, *Streptococcus faecalis*, *Clostridium butyricum*, *Bacillus mesentericus*, *Bacterium lacticum*, *Enterococcus faecalis*, *Bacillus subtilis*, *Bacillus acidophilus*) were investigated and it was found that probiotics were found to be effective in the treatment of MHE. Most of these studies evaluated MHE using the number connection test (NCT). In all studies, probiotics were shown to be superior in preventing progression to OHE and improving MHE compared to the placebo or no treatment group. In studies comparing probiotics with lactulose, better results were obtained in the NCT test in the lactulose treatment group compared to the probiotic treatment group.[23,24] In another study evaluating the efficacy of probiotics in the treatment of MHE, it was found that *Clostridium butyricum* and *Bifidobacterium infantis* were effective in improving MHE in patients with cirrhosis due to HBV.[25] In the prospective study conducted by Goyal et al.[26] after 3 months of rifaximin and lactulose treatment of patients with MHE, a significant improvement was found in MHE. Relapse was observed in 50% of the patients six months after discontinuation of treatment.[26]

In our study, the treatment efficacy for MHE was found to be higher in the groups given lactulose and LbGG compared to the placebo group. There was a statistically significant increase in the CFF test values in both groups. But there is no statistical difference between LbGG and lactulose. The reason why there was no difference between probiotics and lactulose may be due to the necessity of receiving treatment for more than 1 month for LbGG colonization in the intestinal flora. The intestinal colonization rate must increase in order for LbGG to be effective, although the effect of lactulose occurs immediately through known mechanisms. No significant parameters were found when factors that could predict benefit from treatment in the treatment groups were analyzed statistically. By increasing the number of patients, clearer conclusions can be drawn about potential factors which can predict treatment success. The fact that only CFF was used for the diagnosis of MHE in our study, the absence of any neuropsychiatric test used, and the shorter treatment period compared to other studies can be considered as limitations of our study.

In this light, it is known that MHE can progress to OHE, increases mortality, morbidity and health expenditures, and lead to a decrease in the driving performance, quality of life, and work performance of patients. Based on the results of our study, it can be suggested that patients with advanced Child-Pugh stage and high MELD scores should be approached more carefully in terms of MHE screening.

CONCLUSION

In the treatment of MHE, LbGG treatment is as effective as lactulose treatment and can be used safely. Also that it is beneficial for patients, especially those who use vehicles-construction machines and have occupations defined as blue-collar jobs, to protect both the patient and the people they serve.

Ethics Committee Approval: Ethics committee approval was received from the Ethics Committee of Gaziantep University (Date: July 24, 2017, Decision no: 2017/280).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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