To Determine the Outcome of Probiotics in Patients of Minimal Hepatic Encephalopathy with Liver Cirrhosis

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ABSTRACT

Background: Minimal hepatic encephalopathy (MHE) is the earliest form of hepatic encephalopathy and can affect up to 80% of cirrhotic patients. Although often not considered to be clinically relevant and, therefore, not diagnosed or treated, MHE has been shown to affect daily functioning, quality of life, driving and overall mortality. In addition to physician reporting and driving restrictions, medical treatment for MHE includes probiotics. Liver transplantation may not result in reversal of the cognitive deficits associated with MHE. **Objective:** The objective of this study was to determine the outcome of probiotics in patients of minimal hepatic encephalopathy with liver cirrhosis. **Study Design:** Descriptive, case series. **Setting:** Department of Medicine, PMC affiliated hospitals, Faisalabad. **Period:** Six months after approval of synopsis from 18/05/2016 to 18/11/2016. **Methodology:** After taking approval from hospital ethical committee, patients coming through OPD fulfilling the inclusion criteria were enrolled and informed consent was taken. All the patients were given probiotics (one capsule of ECOTEC™, three times a day) for 3 months. Development of overt hepatic encephalopathy was assessed clinically within 3 months of treatment by using West Haven criteria as per operational definition. Follow up was done by taking patient's contact number. **Results:** In our study, out of 120 cases, 55.83%(n=67) were between 20-50 years of age while 44.17%(n=53) were between 51-70 years of age, mean±sd was calculated as 47.21±12.78 years, 36.67%(n=44) were male and 63.33%(n=76) were females, mean duration of disease was calculated as 6.82±1.84 months, frequency of development of overt hepatic encephalopathy was recorded in 22.5%(n=27). **Conclusion:** We concluded that the outcome of probiotics is not poor in patients of minimal hepatic encephalopathy with liver cirrhosis.

Keywords: Liver cirrhosis, treatment, probiotics, minimal hepatic encephalopathy

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INTRODUCTION

Hepatic encephalopathy (HE) is a common and usually reversible neurocognitive syndrome occurring in patients with cirrhosis.[1] It manifests as a spectrum of changes from minimal HE (MHE), which is a state of low-level cognitive dysfunction detectable in up to 70% of the patients, to an overt HE, which has the risk of cerebral edema and death.[2] MHE is a complex neuropsychological complication of cirrhosis, which is characterized by delayed reaction time and abnormal response inhibition. MHE significantly interferes with the normal functioning of daily routine activity, and also impairs health-related quality of life (HRQOL).[3, 4]

The pathogenesis of MHE is multifactorial and the exact mechanisms causing brain dysfunction are still unknown. Increased blood ammonia is present in about 90% of the patients and is considered to play a major role. Ammonia is produced mainly in the gastrointestinal tract by enterocytes from glutamine and by colonic bacterial catabolism of nitrogenous sources.[2]

Then, it enters the circulation via the portal vein and is converted into urea by the liver. Intestinal flora produces toxins, which may aggravate the development of HE by increasing the toxicity of ammonia.[5]

Probiotics may have multiple beneficial effects in the treatment of minimal HE. In principle, probiotics may exhibit efficacy in the treatment of hepatic encephalopathy by decreasing total ammonia level in the portal blood and decreasing inflammation and oxidative stress in the hepatocytes leading to increased hepatic clearance of ammonia and other toxins.[6] Probiotics are effective in secondary prophylaxis of HE.[7]

In literature there is contrary results regarding the development of overt hepatic encephalopathy by using probiotics. In one study development of overt hepatic encephalopathy after taking probiotics was 34.4%.[8] In another study, it was 15.1%.[7] In a systemic review, Bajaj et al noted that no patient (0%) of MHE developed overt hepatic encephalopathy after the treatment with probiotics.[5] Treatment of hepatic encephalopathy is a clinical problem for physicians. Probiotics is not used in routine practice for the prevention of development of overt hepatic encephalopathy and there is no local data available on this topic. As, there is controversy in literature, regarding the use of probiotics in treatment of MHE. So, the results of my study will be helpful in selecting a proper treatment modality as a first line of treatment for minimal hepatic encephalopathy with liver cirrhosis so that severity of this disease can be controlled.

METHODOLOGY

Study Design: Descriptive, case series

Settings: Department of Medicine, PMC affiliated hospitals, Faisalabad.

Period: One year from 01-12-2015 to 30-11-2016

Sample Size: By using WHO sample size calculator for single proportion

- P = 15.1%[6]
- Absolute precision required = 6%
- Confidence level = 95 %
- Sample size = 120

Sample Technique: Non-probability consecutive.

Inclusion Criteria:

- Both male and female patient age ranges from 20-70 years.
- Patients having minimal hepatic encephalopathy in liver cirrhotic patients (as per operational definition).

Exclusion Criteria:

- Patients with overt HE or a history of overt HE in the past 6 weeks
- History of alcohol intake during past 6 weeks
- History of antibiotic or lactulose or probiotics use within the past 3 weeks
- Gastrointestinal bleed in the past 6 weeks
- History of recent use of drugs (<6 weeks) effecting psychometric performance, such as anti-depressants, antiepileptic, sedatives, psychotropic drugs
- Renal insufficiency with creatinine >1.5 mg/Dl

DATA COLLECTION PROCEDURE

After taking approval from hospital ethical committee, patients coming through OPD fulfilling the inclusion criteria were enrolled and informed consent was taken. All the patients were given probiotics (one capsule of ECOTEC™, three times a day) for 3 months. Development of overt hepatic encephalopathy was assessed clinically within 3 months of treatment by using West Haven criteria as per operational definition. Follow up was done by taking patient's contact number. All the information was collected on a specially designed proforma (attached) by me.

DATA ANALYSIS

The data was entered and analyzed in SPSS version 20. Descriptive statistics including mean and standard deviation of numerical values like age and duration of liver cirrhosis was evaluated. Frequency and percentage was calculated for qualitative variable like gender and development of overt hepatic encephalopathy. Development of overt hepatic encephalopathy was compared by using chi-square test. Effect modifiers like age, gender and duration of liver cirrhosis were controlled by stratification. Post-stratification chi-square test was applied. P-value ≤ 0.05 was considered significant.

RESULTS

A total of 120 cases fulfilling the inclusion/exclusion criteria were enrolled to determine the outcome of probiotics in patients of minimal hepatic encephalopathy with liver cirrhosis.

Age distribution shows that 55.83%(n=67) were between 20-50 years of age while 44.17%(n=53) were between 51-70 years of age, mean±sd was calculated as 47.21±12.78 years. (Table No. 1)

Table 1: Age distribution (n=120)

Age (in years)	No. of patients	%
20-50	67	55.83
51-70	53	44.17
Total	**120**	**100**
Mean±SD	**47.21±12.78**	

Gender distribution shows that 36.67%(n=44) were male and 63.33%(n=76) were females. (Table No. 2)

Table 2: Gender distribution (n=120)

Gender	No. of patients	%
Male	44	36.67
Female	76	63.33
Total	**120**	**100**

Mean duration of disease was calculated as 6.82±1.84 months. (Table No. 3)

Table 3: Duration of disease (n=120)

Duration of disease (months)	Mean	SD
	6.82	1.84

Frequency of development of overt hepatic encephalopathy was recorded in 22.5%(n=27) while 77.5%(n=93) had no findings of the morbidity. (Table No. 4)

Table 4: Frequency of development of overt hepatic encephalopathy (n=120)

Overt Hepatic encephalopathy	No. of patients	%
Yes	27	22.5
No	93	77.5
Total	**120**	**100**

Effect modifiers like age, gender and duration of liver cirrhosis were controlled by stratification. Post-stratification chi-square test was applied. P-value ≤0.05 was considered significant. (Table No. 5-7)

Table 5: Stratification for frequency of development of overt hepatic encephalopathy with regards to age

Age (in years)	Overt Hepatic Encephalopathy		P value
	Yes	No	
20-50	13	54	0.36
51-70	14	39	

Table 6: Stratification for frequency of development of overt hepatic encephalopathy with regards to gender

Gender	Overt Hepatic Encephalopathy		P value
	Yes	No	
Male	9	35	0.68
Female	18	58	

Table 7: Stratification for frequency of development of overt hepatic encephalopathy with regards to duration of disease

Duration of disease	Overt Hepatic Encephalopathy		P value
	Yes	No	
1-8 weeks	8	62	0.0006
>8 weeks	19	31	

DISCUSSION

Minimal hepatic encephalopathy (MHE) is the earliest form of hepatic encephalopathy and can affect up to 80% of cirrhotic patients. Although often not considered to be clinically relevant and, therefore, not diagnosed or treated, MHE has been shown to affect daily functioning, quality of life, driving and overall mortality. In addition to physician reporting and driving restrictions, medical treatment for MHE includes probiotics. Liver transplantation may not result in reversal of the cognitive deficits associated with MHE.

Probiotics is not used in routine practice for the prevention of development of overt hepatic encephalopathy and there is no local data available on this topic. As, there is controversy in literature, regarding the use of probiotics in treatment of MHE. So, the results of this study are helpful in selecting a proper treatment modality as a first line of treatment for minimal hepatic encephalopathy with liver cirrhosis so that severity of this disease can be controlled.

In our study, frequency of development of overt hepatic encephalopathy was 22.5%(n=27).

We compared our results with previous literature where a study reveals that development of overt hepatic encephalopathy after taking probiotics was 34.4%.[8] In another study, it was 15.1%.[7] In a systemic review, Bajaj et al noted that no patient (0%) of MHE developed overt hepatic encephalopathy after the treatment with probiotics.[5] The findings of our study are in agreement with those of showing 34.4%[8] and 15.1%[7] our findings are in between of these findings being 22.5% of the cases of developed MHE.

Xu J and others[9] in a meta-analysis ruled out the role of probiotics on liver cirrhotic patients with hepatic encephalopathy and recorded that six randomized controlled trials involving 496 liver cirrhotic patients were included. The results showed that probiotic therapy significantly reduced the development of overt hepatic encephalopathy (OR [95% CI]: 0.42 [0.26, 0.70], P=0.0007). However, probiotics did not affect mortality, levels of serum ammonia and constipation (mortality: OR [95% CI]: 0.73 [0.38, 1.41], P=0.35; serum ammonia: WMD [95% CI]: -3.67 [-15.71, 8.37], P=0.55; constipation: OR [95% CI]: 0.67 [0.29, 1.56], P=0.35). They concluded that probiotics decrease overt hepatic encephalopathy in patients with liver cirrhosis.

Sammy Saab and others[10] evaluated the efficacy of probiotics in the management minimal hepatic encephalopathy (MHE) and overt HE (OHE) in comparison to no treatment/placebo and lactulose and concluded that overall the use of probiotics was

more effective in decreasing hospitalization rates, improving MHE and preventing progression to OHE in patients with underlying MHE than placebo, but similar to that seen with lactulose. The use of probiotics did not affect mortality rates.

In summary, the results of this study are helpful in selecting a proper treatment modality as a first line of treatment for minimal hepatic encephalopathy with liver cirrhosis so that severity of this disease may be controlled.

CONCLUSION

We concluded that the outcome of probiotics is promising in patients of minimal hepatic encephalopathy with liver cirrhosis.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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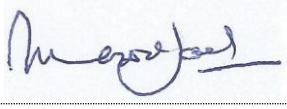
Dr. Masood Javed Associate professor of Medicine PMC / DHQ Hospital, Faisalabad	Analysis the data & Drafting the article	
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