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COMPARISON OF RIFAXIMIN WITH PLACEBO FOR THE TREATMENT OF HEPATIC ENCEPHALOPATHY

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ABSTRACT

Aim: Comparison of Rifaximin with placebo for the treatment of hepatic encephalopathy **Methods:** A total of 150 cases (75 in Rifaximin and 75 in placebo group) presenting with liver cirrhosis and grade IV of hepatic encephalopathy in both gender and aging more than 20 years were enrolled in this study from Emergency/Outpatient Department of Medicine. Before randomization of patients in two groups (Rifaximin and Placebo), verbal consent of the participants was obtained for inclusion their data in this trial. We assured to keep their data confidential. After starting standard treatment to all the cases i.e. Lactulose 30ml 4 times a day, Bowel wash, oral Metronidazole 250mg TDS. Rifaximin group was advised for 550mg twice a day for one week while placebo group was advised 5% D/W1000cc. The patients were followed up to record the recurrence i.e. development of hepatic encephalopathy within 3 months of treatment. **Results:** In this study, out of 150 cases in Rifaximin Group, 30.67%(n=23) and 36%(n=27) were between 20-50 years of age while 69.33%(n=52) in Rifaximin and 64%(n=48) in Placebo Group were between 51-80 years of age, mean + SD was calculated as 54.42±9.21 years and 56.14±10.81 years respectively, 49.33% (n=37) in Rifaximin and 45.33%(n=34) in Placebo Group were males whereas 50.67%(n=38) in Rifaximin and 54.67% (n=41) in Placebo group were males. On comparison of both groups, we found recurrence rate as 28% in Rifaximin and 53.33% in Placebo group, p value was 0.002 showing a significant lower rate in Rifaximin group. **Conclusion:** The use of rifaximin shows significantly lower rate of recurrence of hepatic encephalopathy when compared to placebo.

KEYWORDS: Hepatic encephalopathy, treatment, Rifaximin, Placebo, recurrence.

INTRODUCTION

Chronic liver disease (CLD) is considered as a global health issue, use of alcohol is the most common cause of CLD in western population, whereas in Pakistan, Hepatitis B & C viruses are responsible for this disease.[1] More than 10% of Asian population is suffering with hepatitis B while the rate for hepatitis C varies 4% to 12%.[2-3]

Chronic liver disease may have a prognostic effect and cause other morbidities including ascites, hepatic encephalopathy, esophageal variceal hemorrhage and hepatorenal syndrome etc.[4] Hepatic encephalopathy is recorded in more than 60% of all cases presenting with cirrhosis, it further include demonstrable abnormalities on psychometric test,[5,6] out of these around 30% of CLD cases die due to hepatic encephalopathy.[7-8] Hepatic encephalopathy is an acute neurological condition may arise secondary to failure of liver. The pathogenesis of this condition is not well-recognized; however, hyperammonemia is known as a causative factor of this condition.[7] The clinical outcome of hepatic encephalopathy varies from interrupted mental status to deep coma.[8]

Usually, HE is diagnosed clinically, however, the diagnosis of covert HE is more challenging being the normal clinical findings in these cases. Varied signs and symptoms like disturbance in sleep-wake cycle is reported in covert HE cases; however, psychometric and neuropsychological tests are used to diagnose it.[9-11] Most of the management modalities for HE reduces the load of nitrogenous in the gut. Some of the oral therapies (antibiotics) including paromomycin, vancomycin, neomycin and metronidazole are used effectively with or without adding lactulose for reduction in load of ammonia producing enteric bacteria in acute HE cases.[12] Rifaximin was introduced as minimally absorbed oral agent, it is a broad-spectrum antibiotic covering gram positive and negative anaerobes and aerobes for the management of HE.[13] However, in this study we intend to record recurrence of HE in cases treated with Rifaximin and compared to placebo, our results will add recent findings regarding efficacy of

Rifaximin in our population which will be helpful while managing HE in this area.

PATIENTS AND METHODS

A total of 150 cases (75 in Rifaximin and 75 in placebo group) presenting with liver cirrhosis and grade IV of hepatic encephalopathy in both gender and aging more than 20 years were enrolled in this study from Emergency/Outpatient Department of Medicine. We excluded all cases with renal failure (proven on lab investigations), diabetic cases and those with acute fulminant of hepatic failure. Before randomization of patients in two groups (Rifaximin and Placebo), verbal consent of the participants was obtained for inclusion their data in this trial. We assured to keep their data confidential. After starting standard treatment to all the cases i.e. Lactulose 30ml 4 times a day, Bowel wash, oral Metronidazole 250mg TDS. Rifaximin group was advised for 550mg twice a day for one week while placebo group was advised 5% D/W1000cc. The patients were followed up to record the recurrence i.e. development of hepatic encephalopathy within 3 months of treatment. We used SPSS-14 for data analysis and to record any significance difference between Rifaximin and placebo group regarding recurrence.

RESULTS

In this study, out of 150 cases in Rifaximin Group, 30.67% (n=23) and 36% (n=27) were between 2050 years of age while 69.33% (n=52) in Rifaximin and 64%(n=48) in Placebo Group were between 51-80 years of age, mean ±SD was calculated as 54.42±9.2 years and 56.14±10.81 years respectively.(Table No. 1) 49.33% (n=37) in Rifaximin and 45.33%(n=34) in Placebo Group were males whereas 50.67%(n=38) in Rifaximin and 54.67% (n=41) in Placebo group were males.

(Table No. 2) On comparison of both groups, we found recurrence rate as 28% in Rifaximin and 53.33% in Placebo group, p value was 0.002 showing a significant lower rate in Rifaximin group. (Fig. 1).

Table 1: Age Distribution (n=150).

Age (in years)	Rifaximin Group (n=50)		Placebo Group (n=50)	
	No. of patients	%	No. of patients	%
20-50	23	30.67	27	36
51-80	52	69.33	48	64
Total	**75**	**100**	**75**	**100**
Mean ± SD	**54.42±9.21**		**56.14±10.81**	

Table 2: Gender Distribution (n=150).

Gender	Group-A (n=75)		Group-B (n=75)	
	No. of patients	%	No. of patients	%
Male	37	49.33	34	45.33
Female	38	50.67	41	54.67
Total	**75**	**100**	**75**	**100**

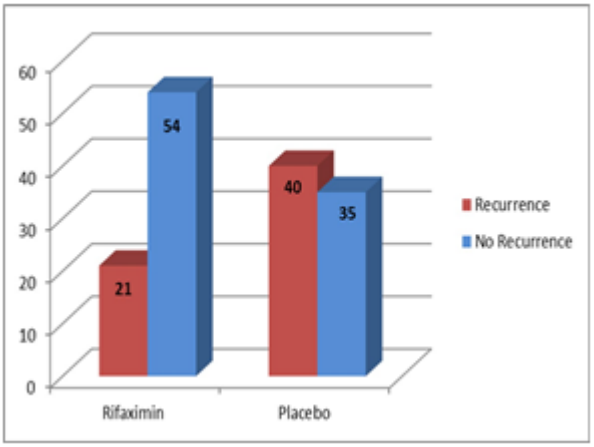

Fig. 1: Comparison of rifaximin to placebo.

DISCUSSION

This study reveals that Rifaximin group had significantly lower rate of recurrence of HE as compared to placebo, these findings are verified by another study[13] where the breakthrough episode of hepatic encephalopathy occurred in 22.1% of patients in the Rifaximin group, as compared with 45.9% of patients in the placebo group while the findings of Steven L[14] are in contrast with the our study who recorded that hepatic encephalopathy in 42% of the patients treated with rifaximin. Mas and others[15] in a prospective study to evaluate the safety and efficacy of rifaximin compared with lactitol for the management of cirrhotic subjects presenting with grade I–III recurrent or acute hepatic encephalopathy. A total of 103 cases were randomized in their study to receive Rifaximin (n: 50, 1200 mg in a day) or lactitol (n: 53, 60 gram in a day) for 5 to 10 days. Demographic data and characteristics of HE were comparable in both groups. Changes in porto-systemic encephalopathy (index on entry and at the end of the study) were used to evaluate the efficacy of the two therapies. The investigators found that both therapies were effective, but a significantly higher effect on electroencephalographic abnormalities and ammonia levels was recorded in cases treated with rifaximin. Another trial compared rifaximin with placebo

and revealed the active therapy significantly improved only asterixis, whilst mental status, PSE index, and intellectual function was not significantly different in both groups.[16]

Our findings in support of other studies clarify that the use of Rifaximin for the management of HE is beneficial and significantly better when compared to placebo group cases.

CONCLUSION

The use of rifaximin shows significantly lower rate of recurrence of hepatic encephalopathy when compared to placebo.

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