

# EFFICACY OF RIFAXIMIN IN HEPATIC ENCEPHALOPATHY

Mustfain Rashid,<sup>1</sup> Kanwal Yasmeen,<sup>2</sup> Zumer Abdul Khaliq<sup>2</sup>

## ABSTRACT

**Background:** Hepatic encephalopathy (HE) is among the commonest complications to present in the medical emergencies due to chronic liver disease (CLD). Multiple regimens have been tried and newer antibiotic like Rifaximin is under extensive discussion regarding its management. **Objective:** To determine the efficacy of rifaximin in cases of chronic liver disease presenting with hepatic encephalopathy. **Methodology:** In this descriptive cases series study, which was conducted at Department of Medicine, Services Hospital, Lahore from 1<sup>st</sup> July to 31<sup>st</sup> December 2016. The cases of both genders with age range of 30–70 years, having CLD (Child Pugh Class B & C) and acute hepatic encephalopathy of grade II or more irrespective of the cause were included in this study. The cases with other co morbid conditions like DM, hypertension, renal or cardiac failure and those taking sedative, were excluded from this study. Hepatic encephalopathy was labeled according to the West Haven Criteria. The cases of HE were given Rifaximin in a dose of 550 thrice a day for 7 days and complete resolution of hepatic encephalopathy at 7<sup>th</sup> day was labeled as positive efficacy. Data was analyzed by using SPSS 20. **Results:** In this study, there were total 300 cases out of which 170 (56.67%) were males and 130 (43.33%) females. There were 150 cases in each child pugh class B and C and 114 (38%) cases had grade IV hepatic encephalopathy. Efficacy of rifaximin was seen in 164 (45.33%) cases. The efficacy was significantly high in cases that had Child Pugh Class B where it was seen in 104 (69.33%) cases as compared to 60 (40%) in class C with p value of 0.03. Efficacy was also significantly better in grade III encephalopathy 70 (72.91%) cases in contrast to 34 (29.82%) cases with grade IV with p= 0.001. **Conclusion:** Rifaximin is good antibiotic for gut flora but it relieves hepatic encephalopathy in only half of cases. It is significantly better in cases with Child pugh class B and with encephalopathy grade III.

**Key words.** CLD, Rifaximin, West Haven Criteria, Hepatic Encephalopathy.

## INTRODUCTION

Liver cirrhosis is one of the most common presentations at the medical and gastroenterology units.<sup>1</sup> It was an irreversible damage of the liver which results in fibrosis and impairment in various function of the liver.<sup>2</sup> Its number is increasing globally especially in developing countries like Pakistan due to increasing number of hepatitis B and C infection.<sup>3</sup> The other causes leading to its development included other viral infections, drugs, toxins, glycogen and iron storage diseases, alcoholism etc.<sup>2-3</sup>

The initial presentation is vague and comprise malaise, nausea, vomiting, but at end stage it can lead to various complications, which have their own appearances.<sup>4</sup> These include hepatic encephalopathy, ascities, hepatorenal syndrome, hepato-pulmonary syndrome, upper GI bleeding and osteoporosis. Hepatic encephalopathy is a well reported and can be a life threatening complication of cirrhosis.<sup>4-5</sup>

There are multiple theories regarding its development.<sup>6,7</sup> The most popular is the ammonia theory which describes that there is increased production of ammonia in such cases by gut flora that surpasses the detoxification capabilities of the liver and cross the blood brain barrier and affect the brain in multiple ways. Secondly there is

another theory regarding imbalance between the ratios of plasma aromatase amino acid to branched chain amino acids. This leads to more of the aromatase amino acid resulting more of such neurotransmitters that can interfere with normal functioning. The other one is GABA receptor inhibition at the post synaptic membrane.<sup>6-8</sup>

Multiple treatment options have been tried and include enema, lactulose, rifaximin, lactilol, metronidazole, neomycin, vancomycin either alone or in difference combinations. Rifaximin is an oral antibiotic, which is not well absorbed in the gut and is used in altering gut flora.<sup>9-12</sup> The objective of this study was to determine the efficacy of rifaximin in cases of chronic liver disease presenting with hepatic encephalopathy.

## METHODOLOGY

In this descriptive cases series study, which was conducted at Department of Medicine, Services Hospital Lahore from 1<sup>st</sup> July to 31<sup>st</sup> December 2016. The cases of both genders, with age range of 30–70 years, having CLD (Child Pugh Class B & C) and acute hepatic encephalopathy of grade II or more irrespective of the cause were included in this study. The cases with other co morbid conditions like DM, hypertension, renal or cardiac failure and those taking sedative were excluded from this study.

1. RHC Bucheki, District Nankana, Pakistan.

2. DHQ Hospital, Sheikhopura, Pakistan.

**Correspondence:** Dr. Mustfain Rashid, Medical Officer, RHC, Bucheki, District Nankana, Pakistan.

**Phone:** +92-333-8363727

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Hepatic encephalopathy was labeled according to the West Haven Criteria. The cases of HE were given Rifaximin in a dose of 550 mg tds for 7 days and complete resolution of hepatic encephalopathy at 7<sup>th</sup> day was labeled as positive efficacy.

The diagnosis of hepatic encephalopathy was made and divided into following grades; Grade I: Trivial lack of awareness, Euphoria or anxiety, shortened attention span impaired performance of addition:

Grade II: Lethargy or apathy Minimal disorientation for time or place, subtle personality change, inappropriate behavior and impaired performance of subtraction.

Grade III: Somnolence to semi-stupor, but responsive to verbal stimuli confusion and gross disorientation

Grade IV: Coma (unresponsive to verbal or noxious stimuli)

The cases having encephalopathy of grade II or more were included in this study. The data was entered and analyzed by using SPSS version 20. Age, duration of cirrhosis was presented as mean and standard deviation. Gender, grade of hepatic encephalopathy, child pugh class and efficacy were presented in frequency and percentages. Post stratification chi square test was used to see statistical significance. P value less than 0.05 was considered as significant.

## RESULTS

In this study, there were total of 300 cases, out of which 170 (56.67%) were males and 130 (43.33%) females. The mean age was 53.17±4.87 years. There were 150 cases in each child pugh class B and C and 114 (38%) cases had grade IV hepatic encephalopathy as in table I.

**Table I: Baseline characteristics in study subjects (n=300) Study variables (n=300)**

Variables	Numbers	Percentage
Male	170	56.67
Female	130	43.33
Child pugh class B	150	50
Child pugh class C	150	50
Grade II encephalopathy	90	30
Grade III encephalopathy	96	32
Grade IV encephalopathy	114	38

Efficacy of rifaximin was seen in 164 (45.33%) cases. The efficacy was significantly high in cases that had Child Pugh Class B where it was seen in 104 (69.33%) cases as compared to 60 (40%) in

class C with p value of 0.03. Efficacy was also significantly better in grade III encephalopathy 70 (72.91%) cases in contrast to 34 (29.82%) cases with grade IV in their respective group with p= 0.001 as in table II.

**Table II: Efficacy of rifaximin with respect to Child Pugh Class and grade of encephalopathy**

Child pugh class vs efficacy			
Child pugh class	Efficacy		Significance
	Yes	No	
B	104 (69.33%)	146 (30.67%)	0.03
C	60 (40%)	90 (60%)	
Child pugh class vs efficacy			
Child pugh class			
II	60 (66.67%)	30 (33.33%)	0.001
III	70 (72.91%)	26 (27.09%)	
IV	34 (29.82%)	80 (70.18%)	

## DISCUSSION

Hepatic encephalopathy is a medical emergency and is the end result of various pathophysiological mechanisms as a result of different insulting events like constipation, GI bleeding, electrolyte disturbance, infections and so on. The mainstay of the treatment lies on two components, removing the insulting agent and sterilization of the gut and hence decreasing the ammonia levels. Lactulose is the most widely used and Rifaximin is the recent one used for this purpose.

Efficacy of rifaximin was seen in 164 (45.33%) cases in the present study. This was almost similar to studies done by Ojetti V et al in the past that also had the efficacy around 50% of their cases.<sup>11</sup> However, the study done by Sharma BC et al,<sup>12</sup> where they compared it with lactulose and it was seen that lactulose had better results than this. Zullo et al<sup>13</sup> also were unable to prove the Rifaximin as better agent than the lactulose in the treatment of hepatic encephalopathy, however the results were not statistically significant.

In the present study, the efficacy of Rifaximin in HE was significantly high in cases that had Child Pugh Class B where it was seen in 104 (69.33%) cases as compared to 40% in class C with p value of 0.03. According to a study done by Bass et al, it was seen that the cases that had more severe disease, they had more chances of HE and it was also seen that these cases were difficult to treat and also had recurrence of hepatic encephalopathy earlier than the cases with milder form of the disease. The severity in our study was labeled by Child Pugh Classification and in their study, they used MELD scoring system. This was

also observed by the study conducted by Neff et al that found that the efficacy with milder form of disease (MELD score less than 20) had better one than severe liver disease.

## CONCLUSION

Rifaximin is good antibiotic for gut flora but it relieves hepatic encephalopathy HE in only half of cases. It is significantly better in cases with Child pugh class B and with encephalopathy grade III.

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