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Research Article

EFFICACY OF RIFAXIMIN IN HEPATIC ENCEPHALOPATHY¹Muneeba Zafar, ²Muhammad Asim Iqbal, ³Luqman Qaiser.

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Abstract:

Objective & methodology: The objective of this study was to determine the efficacy of rifaximin in cases of chronic liver disease presenting with hepatic encephalopathy. In this descriptive cases series study, which was conducted at Sir Ganga Ram Hospital Lahore, Sharif Medical City Lahore and DHQ hospital, Gujranwala from May 2018 to December 2018. 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, HTN, 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 mg tds for 7 days and complete resolution of hepatic encephalopathy at 7th day was labeled as positive efficacy.

Results: In this study there were total 150 cases out of which 85 (56.67%) were males and 65 (43.33%) females. The mean age was 55.34±5.12 years. There were 75 cases in each child pugh class B and C and 57 (38%) cases had grade IV hepatic encephalopathy. Efficacy of rifaximin was seen in 82 (45.33%) cases. The efficacy was significantly high in cases that had Child Pugh Class B where it was seen in 52 (69.33%) cases as compared to 40% in class C ($p=0.03$). Efficacy was also significantly better in grade III encephalopathy affecting 35 (72.91%) cases in contrast to 17 (29.82%) cases with grade IV in their respective group with $p= 0.001$.

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

Key words: HE, CLD, Rifaximin, West Haven Criteria

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INTRODUCTION:

Liver cirrhosis is the end result of liver damage and is defined by the development of the fibrosis and nodules due to chronic liver injuries and repair mechanism. There are various causes of liver injury including drugs, toxins, infections, malignancies etc. It is marked as the 12th leading caused of deaths and every year more than 27 thousand deaths are reported in USA. [1] Hepatitis B and C are the most common causes of this in Pakistan comprising 4.3% and 5-8% respectively. [2-4]

End stage liver disease can lead to various complications like ascites, portal hypertension, hepatic encephalopathy (HE), variceal hemorrhage etc. with different degree of severity among different cases. Hepatic encephalopathy is one of the dreadful complications. The clinical spectrum varies from sleep disturbance and mild behavioral changes to overt coma and eventually can end up in death. [5]

The pathophysiology relies upon the ammonia effect on the brain as it is neurotoxin and impairs energy consumption of brain and halts nerve potential transmission through synapses. The diagnosis of HE is made clinically using West Haven Criteria (WH). [6-7] Various Pharmacological agents have been tried in the past for treatment of hepatic encephalopathy. Lactulose is being mostly employed, as it is cheap, effective and easily available. Other agents used a gut sterilizing agents are metronidazole, vancomycin, oral neomycin and quinolones. Rifaximin is a bactericidal agent and have broad-spectrum antibiotic properties. [8-10]

Objective:

To determine the efficacy of rifaximin in cases of chronic liver disease presenting with hepatic encephalopathy.

METHODS:

In this descriptive cases series study, which was conducted at Sir Ganga Ram Hospital Lahore, Sharif Medical City Lahore and DHQ hospital, Gujranwala from May 2018 to December 2018. 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, HTN, 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 mg tds for 7 days and complete resolution of hepatic encephalopathy at 7th day was labeled as positive efficacy.

Hepatic encephalopathy (West Haven Criteria):

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 Impaired performance of subtraction

Grade III: Somnolence to semi-stupor, but responsive to verbal stimuli Confusion 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.

Statistical analysis:

The data was entered and analyzed 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 150 cases out of which 85 (56.67%) were males and 65 (43.33%) females. The mean age was 55.34±5.12 years. There were 75 cases in each child pugh class B and C and 57 (38%) cases had grade IV hepatic encephalopathy as in table 1. Efficacy of rifaximin was seen in 82 (45.33%) cases as in figure 1. The efficacy was significantly high in cases that had Child Pugh Class B where it was seen in 52 (69.33%) cases as compared to 40% in class C as in table 2 with p value of 0.03. Efficacy was also significantly better in grade III encephalopathy affecting 35 (72.91%) cases in contrast to 17 (29.82%) cases with grade IV in their respective group with p= 0.001 as in table 3.

Table 01 : Study variables

VARIABLES	Numbers	%
Male	85	56.67
Female	65	43.33
Chile pugh class B	75	50
Chile pugh class B	75	50
Grade II encephalopathy	45	30
Grade III encephalopathy	48	32
Grade IV encephalopathy	57	38

Figure 1: Efficacy of Rifaxamin n= 150

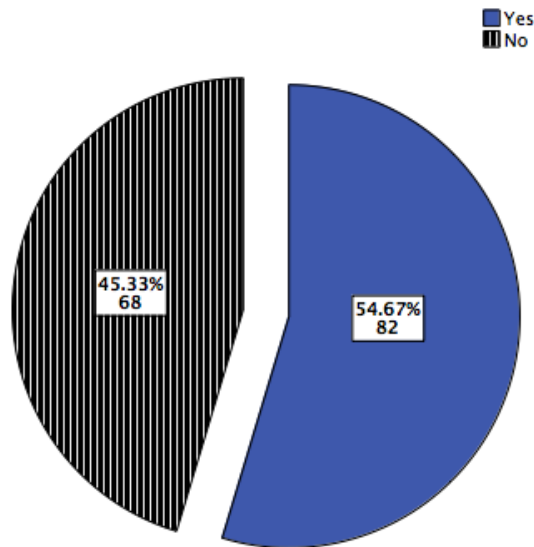


TABLE 02: Efficacy of rifaxamin with respect to Child Pugh Class n= 150

Child pugh class	Efficacy		Significance
	Yes	No	
B	52 (69.33%)	23 (30.67%)	p= 0.03
C	30 (40%)	45 (60%)	

TABLE 03: Efficacy of rifaxamin with respect to Grade of encephalopathy n= 150

Grade of encephalopathy	Efficacy		Significance
	Yes	No	
II	30 (66.67%)	15 (33.33%)	p= 0.001
III	35 (72.91%)	13 (27.09%)	
IV	17 (29.82%)	40 (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 82 (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. [11] However, the study done by Sharma BC et al, where they compared it with lactulose and it was seen that lactulose had better results than this. Zullo et al 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. [12-13]

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 52 (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. [14] 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. [15]

CONCLUSION:

Rifaximin is good antibiotic for gut flora but it relieve 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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