

EFFICACY OF RIFAXIMIN IN HEPATIC ENCEPHALOPATHY

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ABSTRACT

Background: Chronic liver disease (CLD) leads to extensive health care burden, due to various complications including hepatic encephalopathy. **Objective:** To determine the efficacy of Rifaximin in hepatic encephalopathy. **Methodology:** This was a descriptive cases series study, which was conducted at Department of Medicine, Sheikh Zayed Hospital, Rahim Yar Khan from 1st January to 31st July 2016. The cases with age 20-60 years and of either sex having chronic liver disease of both Child Pugh Class B & C presenting with acute hepatic encephalopathy of grade II or more within 1 week diagnosed according to west haven criteria were included in this study. Rifaximin was administered at a dose of 550 mg three times a day for 1 week. Efficacy was labeled as yes when there was complete resolution of symptoms of hepatic encephalopathy with 7 days of administration of the drug. The data was analyzed by using SPSS version 21. **Results:** In study there were 80 cases out of which 57 (71.25%) were males and 23 (28.75%) females. The mean age was 53.23±4.81 years. There were 58 (72.50%) cases in child pugh class C and 22 (27.50%) in class B and 37 (46.25%) has grade IV encephalopathy. Efficacy of Rifaximin was seen in 34 (42.50%) of cases. It was significantly high in child class B where it was observed in 12 (54.55 %) cases as compared to 22 (37.93%) cases in Class C. (P= 0.01). Efficacy was better in those with grade II hepatic encephalopathy where it was seen in 5 (62.50%) out of 8 cases, followed by 16 (45.71%) out of 35 cases in grade III and 13 (35.14 %) out of 37 cases, having grade IV encephalopathy. (P=0.001) (P= 0.001). **Conclusion:** Rifaximin is being used for the treatment of hepatic encephalopathy and it has shown significant better results in Child pugh class B and grade II encephalopathy.

Key words: CLD, West Haven Criteria, Hepatic encephalopathy, Rifaximin.

INTRODUCTION

Chronic liver disease (CLD) causes liver damage and the most feared outcome is end stage liver disease and fibrosis.¹ There are multiple causes of liver injury including infections (hepatitis B, C and other viruses), toxins, drugs, malignancies, glycogen and other mineral deposition disorders.¹ In developing countries like Pakistan, Hepatitis B and C are the most common causes of CLD.^{2,4} Chronic liver disease can lead to various complications like portal hypertension, ascites, variceal hemorrhage, hepatic encephalopathy (HE) and osteoporosis. There is no definitive course of these complications to develop in cases of CLD, and any complication can proceed than the other. There is wide range of clinical spectrum that can vary from a mere sleep disorder 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 coma leading to risk of aspirations and other superadded infections due to hospital stay and bed sores in cases of hospitalized and poor nursing care is one important causes leading to death. 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 vancomycin, metronidazole, quinolones and oral neomycin. Rifaximin is an oral bactericidal agent and being recently used for this. It has a broad-spectrum antibiotic properties.^{8,10} The objective of this study was to determine the efficacy of Rifaximin in hepatic encephalopathy.

METHODOLOGY

Setting; Department of Medicine, Sheikh Zayed Hospital, Rahim Yar Khan. **Duration** 1st January to 31st July 2016. **Sampling technique:** Non-probability consecutive sampling, technique was used to select 80 cases having hepatic encephalopathy. **Inclusion criteria** followed was; both sexes, age 20- 60 years, CLD of Child Pugh Class B & C and Hepatic encephalopathy of grade II or more according to west haven criteria.

Hepatic encephalopathy (West Haven Criteria): is agreed as; 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

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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, and Grade IV: Coma (unresponsive to verbal or noxious stimuli). Rifaxamin was administered at a dose of 550 mg three times a day for 1 week and the cases were assessed daily. Efficacy was labeled as "yes" when there was complete resolution of symptoms of hepatic encephalopathy with 7 days of administration of the drug. The follow up was terminated if the efficacy was seen before the 7th day.

Exclusion criteria; The cases with end stage renal or cardiac disease, cases with co morbid conditions like DM, hypertension and Alcoholics and drug addicts. The data was entered and analyzed using by IBM-SPSS version 21. The data was stratified against the confounding variables. Post stratification chi square test was applied and p value less than 0.05 was considered as significant.

RESULTS

In this study there were 80 cases out of which 57 (71.25%) were males and 23 (28.75%) females. The mean age was 53.23±4.81 years. There were 58 (72.50%) cases in child pugh class C and 22 (27.50%) in class B, and 37 (46.25%) has grade IV encephalopathy. Efficacy of Rifaxamin was seen in 34 (42.50%) of cases. It was significantly high in child class B where it was observed in 12 (54.55 %) cases as compared to 22 (37.93%) cases in Class C. (P=0.01) (Table I). Efficacy was better in those that has grade II hepatic encephalopathy where it was seen in 5 (62.50%) out of 8 cases, followed by 16 (45.71%) cases out of 35 in grade III and 13 (35.14 %) cases in grade IV encephalopathy. (P=0.001) (Table II).

Table I: Efficacy of Rifaxamin versus Child Pugh Class (n= 80)

Child pugh class	Efficacy		Total	Significance P value
	Yes	No		
B	12 (54.55 %)	10 (45.45%)	22 (27.50%)	p= 0.01
C	22(37.93%)	36 (62.07%)	58 (72.50%)	
Total	34 (42.50%)	46 (57.50%)	80 (100%)	

Table II: Efficacy of Rifaxamin versus Encephalopathy Grade (n= 80)

Grade of Encephalopathy	Efficacy		Total	Significance P value
	Yes	No		
II	5 (62.50%)	3 (37.50%)	8 (10%)	p= 0.001
III	16 (45.71%)	19 (54.29%)	35 (43.75%)	
IV	13 (35.14 %)	24 (64.86%)	37 (46.25%)	
Total	34 (42.50%)	46 (57.50%)	80 (100%)	

DISCUSSION

Hepatic encephalopathy is considered as 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.^{11,12} 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 Rifaxamin is the recent one used for this purpose. Efficacy of Rifaxamin was seen in 34 (42.50%) of cases in this study. This finding was consistent with the study done by Ojetti V et al, where the efficacy was seen in less than 50% of the cases.¹¹ The results were slightly poor in our study, which can be explained by the factor that the majority of the cases in the present study were in severe form of the disease i.e. Child pugh class C and grade IV encephalopathy, which both revealed poor results as compared to the rest of the categories. The results of the present study were reinforced by the study of Sharma BC et al,⁹ where they compared Rifaxamin with lactulose and it was observed that the efficacy of Rifaxamin was flowerer than the lactulose. They compared this data to look for time taken to come out of the encephalopathy. Zullo et al also had equivocal results for the efficacy of Rifaxamin when comparing this to lactulose in the treatment of hepatic encephalopathy.¹²⁻¹³

Efficacy of Rifaxamin was seen in 34 (42.50%) of cases. It was significantly high in child class B where it was observed in 12 (54.55 %) cases as compared to 22 (37.93%) cases in Class C with p= 0.01. Efficacy was also better seen in those that has grade II hepatic encephalopathy compared to the other groups with p= 0.001. This was also proved by the study carried out by Bass et al.¹⁴ that also revealed the same results and has shown significant better results. This can be explained by the same pathophysiological

mechanism that more the severe form of the disease and higher are the chances to develop severe complications and more time taken to cope with this complication. It was also observed 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 There was slight difference in terms of assessment of the severity in the present study was labeled by Child Pugh Classification and in their study, they used MELD scoring system. Neff et al,¹⁵ carried the similar study and they also found that the efficacy with milder form of disease (MELD score less than 20) had better outcome in the management of hepatic encephalopathy with Rifaximin than severe liver disease.

CONCLUSION

Rifaximin is being used in the recent times for the treatment of hepatic encephalopathy and it has shown significant better results in Child pugh class B and grade II encephalopathy.

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