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Research Article

### TO DETERMINE THE EFFECTIVENESS OF RIFAXIMIN FOR HEPATIC ENCEPHALOPATHY PATIENTS WITH CHRONIC LIVER DISEASE

<sup>1</sup>Dr Sara Mandokhail, <sup>2</sup>Dr Kaynat Fatima, <sup>3</sup>Dr Rabia Nasir Kakar

<sup>1,2,3</sup> Quetta Institute of Medical Sciences, Quetta.

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**Abstract:**

**Objective:** Hepatic encephalopathy (HE) is a reversible neuro-mental disorders related with ceaseless and intense liver brokenness. It is portrayed by subjective and engine shortfalls of fluctuating seriousness. Aim of the study was to evaluate the effects and outcomes of rifaximin for the treatment of hepatic encephalopathy with chronic liver disease patients.

**Study Design:** Prospective/Randomized controlled trial study.

**Place and Duration of Study:** This study was conducted at the Department of Medicine, Civil Hospital Quetta from March 2020 to March 2020.

**Materials and Methods:** Eighty four patients of both genders whom were diagnosed with hepatic encephalopathy with chronic liver disease were including in this study. All the patients were divided into two groups, Group A included 42 patients and received treatment rifaximin with lactulose, Group B (control group) included 42 patients receiving placebo with lactulose. Follow-up was taken at 15 days or at discharge. Hepatic encephalopathy index and Child-Turcotte-Pugh (CTP) score and model for end-stage liver disease (MELD) were recorded to examine the outcome of treatment.

**Results:** In group A 30 patients were males and 12 were females while in Group B, 32 patients were males and 10 patients were females. In Group A, 34 patients were ages <60 years while 8 patients had ages >60 years, In Group B, 33 patients were ages <60 years and 9 patients were ages >60 years. At start of treatment Child-Turcotte-Pugh\_score p-value 0.467 and model for end-stage liver disease index p-value 0.874 were not statistically significant difference between two groups. Toward the finish of treatment there was noteworthy distinction discovered identified with hepatic encephalopathy file p-esteem 0.039 and model for end-stage liver ailment file p-esteem <0.05 than fake treatment gathering. Youngster Turcotte-Pugh score 0.621 was additionally lower in rifaximin bunch than Group B.

**Conclusion:** The use of rifaximin with lactulose for the treatment of hepatic encephalopathy resulted better outcome than placebo with respect to model for end-stage liver disease index and hospital stay.

**Key Word:** Rifaximin, Chronic liver disease, Hepatic encephalopathy

**Corresponding author:****Dr Sara Mandokhail**

Quetta Institute of Medical Sciences, Quetta.

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**INTRODUCTION:**

Hepatic encephalopathy (HE) is a reversible neuro-mental disorders related with ceaseless and intense liver brokenness. It is portrayed by subjective and engine shortfalls of fluctuating seriousness. Early manifestations incorporate inversion of rest design, lack of care, hypersomnia, peevishness and individual disregard. In later stages, daze and unconsciousness can emerge with neurologic signs including hyperreflexia, unbending nature, myoclonus, and asterixis.[1] The pathophysiology of HE is mind boggling and it shows with dynamic disintegration of the predominant neurological capacities. Hepatic encephalopathy happens within the sight of inadequate hepatic leeway of poisons ingested from the digestive tract bringing about neurochemical anomalies over the blood mind barrier.[2] Elevated serum smelling salts level is the best portray reason for HE and is identified in 60%-80% of influenced patients. [3,4] Current treatment systems are planned for diminishing the serum level of ammonia. [5] This is finished by presenting operators that decrease or restrain creation of intestinal alkali or limit its assimilation from the gastrointestinal tract just as adjusting hastening components, for example, gastrointestinal discharge, electrolyte lopsided characteristics and blockage, contamination, prerenal azotemia, hypokalaemic alkalosis, stoppage, hypoxia, hypovolemia or the utilization of narcotics and tranquilizers. [6] various medications have been attempted either separately or in blend of at least two and in correlation with fake treatments too. These included lactulose, lactitol, anemas, dietary limitation of dietary protein and oral anti-infection agents as metronidazole, neomycin, vancomycin, rifaximin, probiotics, amino acids and different minerals have been attempted. They have indicated diverse level of viability. Anyway metronidazole, lactulose and douche are the most regularly utilized. Rifaximin is an oral anti-infection which isn't invested in the gut and has indicated great efficacies in adjusting gut flora. [7-10] On the other hand, rifaximin is an ineffectively consumed expansive range antimicrobial with not many foundational symptoms and at okay of prompting bacterial resistance. [11,12] These properties make rifaximin a perfect anti-infection for the treatment of patients with HE as a few investigations have demonstrated a noteworthy lessening in plasma smelling salts levels 18-20 with

negligible effect on the ordinary gastrointestinal flora.[13]

This study was conducted aimed to analyze the outcome of rifaxime in chronic liver disease patients, so that better treatment could be provided and to reduce the morbidity and mortality rate of chronic liver disease patients.

**MATERIALS AND METHODS:**

This study was conducted at the Department of Medicine, Civil Hospital Quetta from March 2020 to March 2020. A total of 84 patients of both genders whom were diagnosed with hepatic encephalopathy with chronic liver diseases were included. All the patients were divided into two groups, Group A included 42 patients and received treatment rifaximin with lactulose, Group B (control group) included 42 patients receiving placebo with lactulose. Patients with heart failure, alcohol users, neurological and patients with severe bad health were excluded. Rifaximin 550mg dosage for two time daily and Group B was put on placebo for 10 days. Follow up was taken at 15 days or at discharge. Hepatic encephalopathy index and protosystemic encephalopathy index was recorded to examine the outcome of treatment. All the statistical data was analyzed by SPSS 20. P-value <0.05 was considered as significant.

**RESULTS:**

In group A 30 (71.43%) patients were males and 12 (28.57%) were females while in group B, 32 (76.19%) patients were males and 10 (23.81%) patient were females. In group A, 34 (80.95%) patients were ages <60 years while 8 (19.05%) patients had ages >60 years, in group B, 33 (78.58%) patients were ages <60 years and 9 (21.43%) patients were ages >60 years (Table 1).

At start of treatment Child-Turcotte-Pugh score p-value 0.467 and model for end-stage liver disease index p-value 0.874 were not statistically significant difference between two groups. At the end of treatment there was significant difference found related to hepatic encephalopathy index p-value 0.039 and model for end-stage liver disease index p-value <0.05 than placebo group. Child-Turcotte-Pugh score 0.621 was also lower in rifaximin group than Group B. [Tables 2-3].

**Table No.1: Basic demographical details of patients**

Variable	Group A	Group B
<b>Gender</b>		
Male	30 (71.43%)	32 (76.19%)
Female	12 (28.57%)	10 (23.81%)
<b>Age (years)</b>		
< 60	34 (80.95%)	33 (78.58%)
≥60	8 (19.05%)	9 (21.43%)

**Table No.2: Comparison of hepatic encephalopathy index at start and end of treatment in both groups**

HE index	Group A	Group B	P-value
<b>HE Grade at start</b>			
0/1/2/3/4/	0/13/26/3/0	0/14/24/4/0	0.87
<b>At end discharge</b>			
0/1/2/3/4/	34/5/2/1/0	20/16/4/2/0	0.04

**Table No.3: Comparison of Child-Turcotte-Pugh (CTP) score and model for end-stage liver disease (MELD) at start and end of treatment between both groups**

Variable	Group A	Group B	P-value
<b>CTP score</b>			
At start of treatment	11.09±3.46	10.73±1.52	0.48
At end discharge	9.37±1.29	9.85±3.12	0.62
<b>MELD Score</b>			
At start of treatment	14.38±2.29	13.85±2.45	0.73
At end discharge	11.25±4.06	10.75±6.12	0.04

**DISCUSSION:**

Liver cirrhosis particularly because of hepatitis B and C is an incredible wellbeing concern and their numbers on the ascent in creating nations where there are lesser wellbeing offices and poor mindfulness. This prompts movement of malady and afterward entanglements like hepatic encephalopathy have been seen which were not overseen forcefully can be lethal. Various pharmacological and non-pharmacological moves have been considered to maintain a strategic distance from this with various level of accomplishment. [14,15]

In this study we found that males patients population was high as compared to females 3:1 in both rifaximine group and placebo group. These results shows similarity to some other studies in which number of male patients population was high as compared to females 75 to 85%. [20,21] We found that there is no significant difference in mean age in both groups. It showed similarity to the study conducted by Paik et al [16] in which there was no significant difference according to mean age and gender in placebo and rifaximin group. In our investigation we found that at enlistment, there was no-critical contrast of HE grade between two groups ( $p=0.87$ ). Toward the finish of treatment, there was

noteworthy distinction of mean HE grade between two groups ( $p=0.04$ ). This outcome like two different examinations directed by Hussain et al<sup>21</sup> and Massa et al [17] where rifaximin treated patients more altogether improved HE grade than lactulose treated patients. In any case, this outcome contrast with other investigation led by Paik et al. indicated the mean HE grade was comparatively diminished inside the examination groups ( $p<0.001$ ). [18]

At development, there was no critical contrast of CTP score mean between two groups ( $p = 0.489$  and  $0.62$  individually). Study directed with respect to utilization of rifaximin demonstrated no noteworthy distinction of CTP score mean between two groups ( $p = 0.404, 0.505$  respectively). [19]

In our investigation, we found that there was huge distinction of methods for length of emergency clinic remain between two groups ( $p=0.008$ ). This outcomes bolster two review audit considers, where rifaximin and lactulose decreased hazard and length of hospitalization. [20]

**CONCLUSION:**

Hepatic encephalopathy in chronic liver disease is a common clinical disorder with high rate of morbidity.

We concluded from this study that rifaximine with lactulose showed better efficacy than lactulose alone for reducing the morbidity associated with hepatic encephalopathy.

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