



Outcome of patients taking rifaxamine Vs lactose in patients with hepatic encephalopathy presenting at tertiary care hospital sukkur

Shahabuddin Rind¹, Bashir Ahmed Chandio², Khalil Ahmed Sanghro³, Abdul Rashid dayo⁴, Yar Muhammad Tunio⁵, Professor Dr Altaf Ahmed shaikh⁶

¹Senior registrar, Gastroenterologist, Gastro department Ghulamm Muhammad Mahar medical college sukkur

²Associate Professor Medicine, Medical unit -II, Ghulam Muhammad Mahar Medical College Sukkur

³Senior Registrar, medical unit 1 Ghulamm Muhammad Mahar medical college sukkur

⁴Assistant Professor, medical unit 1, Ghulamm Muhammad Mahar medical college sukkur

⁵Assistant Professor Medicine Department, Gambat Institute of Medical Sciences Gambat Khairpur

⁶Professor and head of department, Medical unit 1 Ghulamm Muhammad Mahar medical college sukkur

Corresponding Author:

Abdul Rashid dayo

Assistant Professor, medical unit 1, Ghulamm Muhammad Mahar medical college sukkur

Email: abdulrasheeddayo960@gmail.com

Abstract

Background: Hepatic encephalopathy is a significant consequence of degenerative chronic liver disease. If not properly controlled, it can lead to higher death rates.

Objective: The objective of this study was to compare the Outcome of patients taking rifaxamine Vs lactose in patients with hepatic encephalopathy presenting at tertiary care hospital sukkur.

Material and method: The current randomized controlled study was conducted at the department of gastroenterology Ghulamm Muhammad Mahar medical college sukkur from January 2023 to January 2024 after taking permission from the ethical board of the institute. A total of 396 individuals of both genders and different aged groups diagnosed with acute hepatic encephalopathy (grade 1 to 3) were included. ⁹ The study participants were randomly assigned to one of two groups: Group A 198 received Rifaxamin 550mg twice day, while Group B 198 received Lactulose 30-90ml daily. Basic demographic information, including name, age, gender, residence, and contact information, were collected. The data was analyzed statistically with SPSS version 16. Quantitative factors such as age were expressed as mean \pm SD. Qualitative characteristics such as gender and improvement in HE grade were presented as frequencies and percentages. The chi-square test was performed to examine the prevalence of improvements in HE grade across both groups. P-values $<$ 0.05 were regarded as significant.



Results: In the current study a total of 196 individuals were enrolled. The study participants were randomly assigned to one of two groups: Group A 198 received Rifaximin 550mg twice day, while Group B 198 received Lactulose 30-90ml daily. Age distribution of participants revealed that 77 (39%) in Group-A and 85 (43%) in Group-B were within 30-50 years of age, while 121 (61%) in Group-A and 113 (57%) in Group-B were within 51-70 years of age. The mean and standard deviation was determined as 44.80+14.72 and 44.23+14.75 years, respectively. The gender distribution of patients was as follows: 101 (49%) in Group-A and 96 (48.4%) in Group-B were men, while 97 (51%) in Group-A and 102 (51.6%) in Group-B were females. Rifaximin and Lactulose improved hepatic encephalopathy grades in 136 (76%) and 131 (72%), respectively. However, 40 (24%) and 49 (28%) in Group-A and Group-B did not demonstrated any improvement, with a p-value of significance >0.05.

Conclusion: The current study concluded that Rifaximin and Lactulose showed equivalent effectiveness in treating mild to severe hepatic encephalopathy

Key word: Outcome; Rifaxamine; lactose; Hepatic encephalopathy

Introduction

Cirrhosis is characterized by the formation of regenerating nodules with fibrous bands in responses to chronic conditions and leads to portal hypertension and end-stage liver disease.¹ Chronic liver disease causes damage to the liver, leading to cirrhosis. It is commonly caused by hepatitis B and C, alcohol use, and fatty liver disease.² Cirrhosis is the 12th biggest cause of mortality by illness, responsible for 27,000 deaths annually in the USA.³ In Pakistan, 4.3% of the population has Hepatitis B, whereas 4.5-8% have Hepatitis C.⁴ Hepatic encephalopathy (HE) is a metabolically generated, possibly reversible brain function disruption that occurs as a consequence of acute or chronic liver illness. It is usually associated with liver cirrhosis.⁵ HE is divided into four classes based on West Haven Criteria (WH).⁶ The etiology of encephalopathy is complex and complicated. Ammonia is quite important in it.⁷ Hepatic encephalopathy is treated with several pharmacological medications. Lactulose is the most often used therapy. Gut decontamination agents include metronidazole, vancomycin, oral neomycin, and quinolones are also prescribed. Rifaximin prevents recurrent hepatic encephalopathy. This non-aminoglycoside antibacterial drug has extensive efficacy against gram-positive and gram-negative aerobic and anaerobic enteric bacteria in vitro as well as in vivo, despite its low absorption. There is insufficient research on the role of rifaximin in acute hepatic encephalopathy, which needs further study. A research found that 76% of patients treated with rifaximin with Lactulose experienced full reversal of HE, but only 50.8% of patients treated with Lactulose alone did so. The study found that therapy with lactulose + rifaximin resulted in a substantial decrease in mortality compared to lactulose and placebo (23.8% vs. 49.1%).⁸ The current study was carried out to find out the Outcome of patients taking rifaxamine Vs lactose in patients with hepatic encephalopathy presenting at tertiary care hospital sukkur

Material and method

The current randomized controlled study was conducted at the department of gastroenterology Ghulam Muhammad Mahar medical college sukkur from January 2023 to January 2024 after taking permission from the ethical board of the institute. A total of 396 individuals of both genders and different aged groups diagnosed with acute hepatic encephalopathy (grade 1 to 3) were included while individuals with Hepatocellular carcinoma, major psychiatric illness and



other metabolic encephalopathy were excluded. The severity of hepatic encephalopathy was assessed using the West Haven Criteria. Improvement in HE was defined as at least one grade decrease in the presenting stage of hepatic encephalopathy following 7 days of therapy.⁹ The study participants were randomly assigned to one of two groups: Group A 198 received Rifaxamin 550mg twice day, while Group B 198 received Lactulose 30-90ml daily. Basic demographic information, including name, age, gender, residence, and contact information, were collected following informed permission. After admission to the ward, participants were tested for baseline hepatic encephalopathy grades & monitored for seven days. Daily assessments were conducted to monitor flapping tremors and mental health state. All information was recorded using a pre-designed Performa. The data was analyzed statistically with SPSS version 16. Quantitative factors such as age were expressed as mean \pm SD. Qualitative characteristics such as gender and improvement in HE grade were presented as frequencies and percentages. The chi-square test was performed to examine the prevalence of improvements in HE grade across both groups. P-values < 0.05 were regarded as significant.

Results

In the current study a total of 396 individuals were enrolled. The study participants were randomly assigned to one of two groups: Group A 198 received Rifaxamin 550mg twice day, while Group B 198 received Lactulose 30-90ml daily. Age distribution of participants revealed that 77 (39%) in Group-A and 85 (43%) in Group-B were within 30-50 years of age, while 121 (61%) in Group-A and 113 (57%) in Group-B were within 51-70 years of age. The mean and standard deviation was determined as 44.80+14.72 and 44.23+14.75 years, respectively as presented in **Table 1**. The gender distribution of patients was as follows: 101 (49%) in Group-A and 96 (48.4%) in Group-B were men, while 97 (51%) in Group-A and 102 (51.6%) in Group-B were females as presented in **table 2**. Cirrhosis was caused by hepatitis C in 358 (90%) individuals, whereas Hepatitis B was identified in 18 (4.5%), Alcoholic cirrhosis in 2% (8), Wilson's disease in 0.5% (2), hemochromatosis in 0.5 percent (2), and autoimmune hepatitis in 0.5% (2). However, the specific etiology was not established in six cases (1.5%). The study eliminated 40 (10%), 22 from group A and 18 from group B, who left the unit within one week. Rifaximin and Lactulose improved hepatic encephalopathy grades in 136 (76%) and 131 (72%), respectively. However, 40 (24%) and 49 (28%) in Group-A and Group-B did not demonstrate any improvement, with a p-value of significance >0.05 as shown in **Table 3**.

Table 1. Age wise distribution of the study population

	Group A N= 198	Group B N= 198
Age in years		
30 to 50	77(39%)	85(43%)
51-70	121(61%)	113(57%)
Mean , SD	44.80+14.72	44.23+14.75

Table 1. Gendre wise distribution of the study population

	Group A N= 198	Group B N= 198
Sex		
Female	97(51%)	102 (51.6%)



Male	101(49%)	96 (48.4%)
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Table 3. Rifaxamin improved grades of hepatic encephalopathy compared to lactulose in individuals with decompensated cirrhosis.

	Group A N= 177	Group B N= 181
Improvement		
Yes	136(76%)	131(72%)
No	40(24%)	49 (28%)

Discussion

Hepatic encephalopathy is a significant consequence of degenerative chronic liver disease. If not properly controlled, it can lead to higher death rates. HE is caused by the liver's failure to detoxify, resulting in elevated blood ammonia levels. The majority of treatments try to reduce ammonia levels. Lactulose & rifaximin are routinely used therapies for people with hepatic encephalopathy. However, long-term usage of lactulose is not recommended due to adverse effects. Rifaximin is gaining popularity as a first-line treatment for reducing recurrent hepatic encephalopathy. This research examined the efficacy of Rifaximin versus lactulose in treating hepatic encephalopathy for 7 days after admission. Hepatitis C was the leading cause of cirrhosis in 90% of individuals, affecting roughly 10 million individuals in Pakistan.¹⁰ In our study 136 (76%) participants in Group-A exhibited improvement from the presenting grades of hepatic encephalopathy, whereas 131 (72%) in Group-B showed improvement. The p-value was determined as >0.05, which was insignificant. Both medications provide similar advantages to individuals. Similar findings were evaluated from the study of Paik et al. when compared rifaximin and lactulose for treating HE. After 7 days of treatment, rifaximin increased HE grades by 81.3% and lactulose by 72.7%, while ammonia levels improved by 78.1% and 59.1%, respectively. There was no significant difference between the two groups (p-value >0.05).¹¹ According to a meta-analysis by Jiang et al. as well as a review by Zullo, Rifaximin is not more effective than lactulose for treating chronic HE.^{12,13} A research at Sheikh Zayd Hospital in Lahore found that Rifaximin did not lessen the risk of recurrent hepatic encephalopathy over a 6-month period.¹⁴ According to Lawrence KR and colleagues, Rifaximin can improve behavioural, biochemical, mental state, and cognitive impairments associated with hepatic encephalopathy.¹⁵ Leevy CB et colleagues observed that rifaximin therapy significantly improved clinical characteristics of encephalopathy compared to non-absorbable disaccharides (lactulose, lactitol). Rifaximin treatment resulted in shorter hospital stays and lower hospital costs compared to lactulose treatment.¹⁶ In a nutshell our study found that rifaximin versus non-absorbable disaccharides had similar effects for individuals with hepatic encephalopathy. We recommend starting with lactulose because to its cheaper cost, and reserving rifaximin for individuals experiencing significant ill effects from disaccharides treatment.

Conclusion

The current study concluded that Rifaximin and Lactulose showed equivalent effectiveness in treating mild to severe hepatic encephalopathy.



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