Original Article

Examine the Efficacy of Rifaximin for Hepatic Encephalopathy Patients with Chronic Liver Disease

Muhammad Uthman[1], Syed Waseem Ahmad Mujtaba[2] and Abdul Matin Qaisar[3]

ABSTRACT

Objective: 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, Shaikh Zayed Hospital Lahore from 1st July 2019 to 31st December 2019.

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

Citation of article: Uthman M, Mujtaba SWA, Qaisar AM. Examine the Efficacy of Rifaximin for Hepatic Encephalopathy Patients with Chronic Liver Disease. Med Forum 2020;31(4):19-22.

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]

[1.] Department of Medicine, Shaikh Zayed Hospital, Lahore.
[2.] Department of Medicine, Amna Inayat Medical College, Sheikhupura.
[3.] Department of Physiology, NM&DC, Sargodha.

Correspondence: Dr. Muhammad Uthman, Associate Professor of Medicine, Shaikh Zayed Hospital, Lahore
Contact No: 0300-4312499
Email: medicalspecialist71@yahoo.com

Received: January, 2020
Accepted: February, 2020
Printed: April, 2020

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 in60%-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, prerenalazotemia, 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, lactilol, 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 anti-microbial 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 levels18-20 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 Department of Medicine, Shaikh Zayed Hospital Lahore from 1st July 2019 to 31st December 2019. 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 10days. 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
Gender		
Male	30 (71.43%)	32 (76.19%)
Female	12 (28.57%)	10 (23.81%)
Age (years)		
< 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
HE Grade at start			
0/1/2/3/4/	0/13/26/3/0	0/14/24/4/0	0.87
At end discharge			
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
CTP score			
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
MELD Score			
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[21] 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.

Author's Contribution:

Concept & Design of Study:	Muhammad Uthman
Drafting:	Syed Waseem Ahmad Mujtaba
Data Analysis:	Abdul Matin Qaisar
Revisiting Critically:	Muhammad Uthman, Syed Waseem Ahmad Mujtaba
Final Approval of version:	Muhammad Uthman

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Mullen K. Hepatic encephalopathy. In: Zakim D, Boyer TD, editors. Hepatology: a textbook of liver disease. 5th ed. Philadelphia, PA: WB Saunders; 2006.p.311–31.
2. Fitz G. Hepatic encephalopathy, hepatopulmonary syndrome, coagulopathy and other complications of chronic liver disease. In: Feldman M, Friedman LS, Sleisenger MH, editors. Sleisenger and Fordtran's Gastrointestinal and Liver Disease. 9th ed. Philadelphia: Saunders Elsevier; 2010.p.1543-55.
3. Ferenci P, Lockwood A, Mullen K, Tarter R, Weissenborn K, Blei AT, et al. Hepatic encephalopathy definition, nomenclature, diagnosis, and quantification: final report of the working party at the11th World Congresses of Gastroenterology, Vienna, 1998. Hepatol 2002; 35:716–20.
4. De Melo RT, Charneski L, Hilas O. Rifaximin for the treatment of hepatic encephalopathy. Am J Health Syst Pharm 2008;65:818–22.
5. Zeneroli ML, Avallone R, Corsi L, Venturini I, Baraldi C, Baraldi M. Management of hepatic encephalopathy: role of rifaximin. Chemotherapy, 2005; 51(Supple 1):90–95.
6. Tarao K, Ikeda T, Hayashi K, Sakurai A, Okada T, Ito T, et al. Successful use of vancomycin hydrochloride in the treatment of lactulose resistant chronic hepatic encephalopathy. Gut 1990; 31:702–706.
7. Sharma BC, Sharma P, Agrawal A, Sarin SK. Secondary prophylaxis of hepatic encephalopathy: an openlabel randomized controlled trial of lactulose versus placebo. Gastroenterol 2009; 137: 885-88.
8. Als-Nielsen B, Gluud LL, Gluud C. Nonabsorbable disaccharides for hepatic encephalopathy. Cochrane Database Syst Rev 2004; CD003044.
9. Les I, Doval E, García-Martínez R. Effects of branchedchain amino acids supplementation in patients with cirrhosis and a previous episode of hepatic encephalopathy: a randomized study. Am J Gastroenterol 2011; 106:1081-88.
10. Ferenci P. Pathogenesis of hepatic encephalopathy. Uptodate, www.uptodate.com (accessed 29 March 2017).
11. Aldridge DR, Tranah EJ, Shawcross DL. Pathogenesis of hepatic encephalopathy: role of ammonia and systemic inflammation. J Clin Exp Hepatol 2015;5(Suppl 1):S7–20.
12. Butterworth RF. Neurosteroids in hepatic encephalopathy: novel insights and new therapeutic opportunities. J Steroid Biochem Mol Biol 2016; 160:94–7.
13. Bajaj JS. The role of microbiota in hepatic encephalopathy. Gut Microbes 2014;5:397–403.
14. Munoz SJ. Hepatic encephalopathy. Med Clin North Am 2008;92:795–812.
15. Bajaj JS, Betrapally NS, Hylemon PB, et al. Salivary microbiota reflects changes in gut microbiota in cirrhosis with hepatic encephalopathy. Hepatol 2015;62:1260–71.
16. Paik YH, Lee KS, Han KH. Comparison of rifaximin and lactulose for the treatment of hepatic

encephalopathy: a prospective andomized study. Yonsei Med J 2005; 46:399–407.
17. Mas A, Rodés J, Sunyer L. Comparison of rifaximin and lactitol in the treatment of acute hepatic encephalopathy: results of a randomized, doubleblind, double-dummy, controlled clinical trial. J Hepatol 2003; 38:51–8.
18. Montagnese S, Middleton B, Mani AR, Skene DJ, Morgan MY. On the origin and the consequences of circadian abnormalities in patients with cirrhosis.Am J Gastroenterol 2010;105(8):1773-81.
19. Bajaj JS, Cordoba J, Mullen KD, et al. Review article: the design of clinical trials in hepatic encephalopathy—an International Society for Hepatic Encephalopathy and Nitrogen Metabolism (ISHEN) consensus statement. Aliment Pharmacol Ther 2011;33:739–47.
20. Vilstrup H, Amodio A, Bajaj J. et al. Hepatic Encephalopathy in Chronic Liver Disease: 2014 Practice Guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. Hepatol 2014;60:715–35.
21. Hussain M, Habib-ur-Rehman, Akhbar K, Ghafoor MB. Hepatic encephalopathy; to compare the efficacy of lactulose alone and lactulose with rifaxamin in patients of hepatic encephalopathy. Professional Med J 2017;24(7):947-951.